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Preparation of *N*-Heterocycles by Radical Cyclisation of Enamides Mediated by Manganese(III) or Copper(I). A Comparison of Cyclisation Methods

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Abstract—Reaction of enamides with manganese(III) acetate or copper(I) chloride/bipyridine has been investigated. In both cases, an initial 5-*endo-trig* radical cyclisation reaction took place to produce functionalised pyrrolidinones. The copper(I)-mediated cyclisations were very efficient and bicyclic dienes could be isolated in >80% yield, while the corresponding manganese(III) reactions were generally more problematic, giving related dienes in lower yield (35–52%).

Introduction

One important method for preparing 5-membered nitrogen heterocycles is the radical cyclisation of unsaturated organohalides.[1] Thus, for example, cyclisations proceeding by a (favoured) 5-*exo-trig* pathway have been shown to provide a mild and flexible approach to a variety of pyrrolidinones.[2] More recently, however, an alternative approach to pyrrolidinones has been developed, which centres on the 5-*endo-trig* radical cyclisation of halo-enamides.[3] This cyclisation is unusual (disfavoured) in that the initial carbamoylmethyl radical reacts to form a 5- rather than a 4-membered (or β-lactam) ring. The (favoured) 4-*exo-trig* cyclisation, to form a β-lactam, is generally observed when radical-stabilising (aromatic) groups are introduced on the enamide C=C bond.[4] These 5-*endo* cyclisations, which can be mediated by tributyltin hydride, have been shown, for example, to provide efficient approaches to substituted pyroglutamates.[5] However, the use of tributyltin hydride is far from ideal as tin-containing by-products are often difficult to remove and the cyclisation leads to the reduction of two functional groups (i.e. the C-halogen and C=C bonds). With a view to developing a more straightforward and versatile approach to functionalised pyrrolidinones, this paper describes the use of manganese(III) or copper(I) reagents as initiators for 5-*endo-trig* radical cyclisations. Both methods have a number of advantages over the use of tributyltin hydride. Hence, the reagents are cheaper, the metal by-products are more easily removed and, importantly, a functional group (generally a double bond or halogen atom) is introduced into the product after cyclisation. Whereas manganese(III)-based cyclisations[6] commonly employ 1,3-dicarbonyl compounds (which readily undergo enolisation), copper(I)-based reactions[7] require precursors with a particularly weak carbon–halogen bond.

Results and Discussion

The formation and reaction of β-amido ester **1** with manganese(III) acetate was first investigated (Scheme 1).[8] This was prepared by *N*-acylation of the imine derived from benzylamine and cyclohexanone, with methyl malonyl chloride. Initial reactions of **1** with manganese(III) acetate in boiling acetic acid, in the presence or absence of copper(II) acetate,[†] were disappointing as a number of unidentifiable products were obtained in trace amounts following column chromatography. However, when the reaction was carried out in boiling methanol (in the absence of copper(II) acetate) diene **2** was isolated. The yield of **2** was found to improve from 10 to 38% when the number of equivalents of manganese(III) acetate was increased from 1 to 4, whereas addition of >4 equiv. was found to have a detrimental effect on the product yield. In order to compare the two different methods of cyclisation, reaction of dichloroamide **3** with copper(I) chloride and bipyridine[‡] was investigated. This was prepared in 79% yield by chlorination of **1**

Keywords: manganese and compounds; copper and compounds; cyclisation; enamides.

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[†] Copper(II) acetate is often used as a co-oxidant in manganese(III)-mediated cyclisations.

[‡] Bipyridine is added to coordinate and solubilise the copper(I) chloride, and alter the redox potential so that reactions can be carried out at reasonable temperatures.

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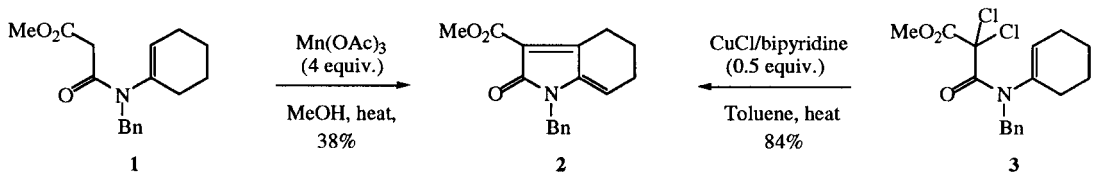
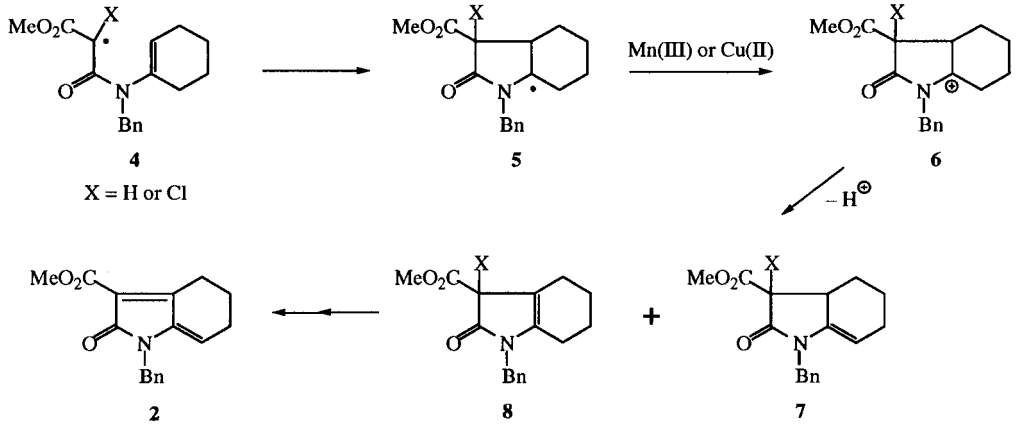


Scheme 1.



Scheme 2.

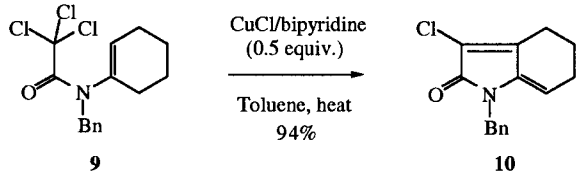
using 2.2 equiv. of sodium hydride and *N*-chlorosuccinimide. Interestingly, on reaction of **3** with 0.5 equiv. of copper(I) chloride/bipyridine in boiling (dry) toluene, diene **2** was also isolated but in a much higher yield of 84% (Scheme 1).

Dichloroamide **3** could also be efficiently cyclised to diene **2** (in 76% yield) using 0.5 equiv. of dichlorotris(triphenylphosphine)ruthenium(II) in boiling toluene. The efficiency of both the copper(I) chloride/bipyridine and ruthenium(II) cyclisation methods compare favourably with related haloamide cyclisations, which have been carried out using nickel in acetic acid[9] or an alternative copper(I) complex (at room temperature).[10]

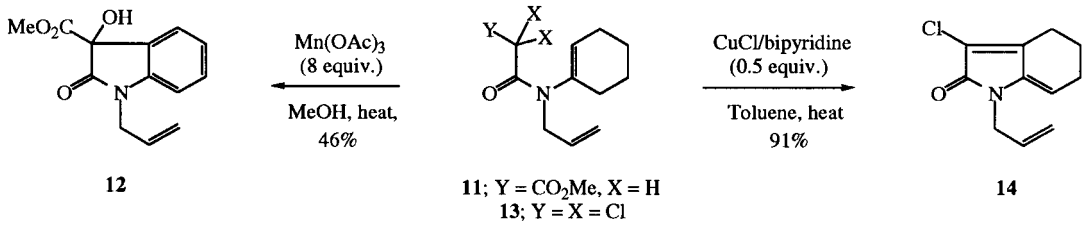
The mechanism of these cyclisation reactions presumably involves initial formation of carbamoylmethyl radical **4** (Scheme 2). Thus, reaction of **1** with manganese(III) is expected to promote an oxidation leading to formal loss of a hydrogen atom (together with manganese(II)), while reaction of **3** with copper(I) (or ruthenium(II)) is expected to lead to chlorine-atom abstraction (and the formation of copper(II)). Radical **4** is then expected to undergo 5-*endo* cyclisation to form tertiary radical **5**, which is particularly susceptible to oxidation by reaction with a further equivalent of manganese(III) or by copper(II). The resultant *N*-acyliminium ion **6** could then undergo deprotonation leading to alkene **7** and/or **8**. Further radical generation/oxidation or loss of HCl (which could be mediated by bipyridine) is then expected to produce diene **2**.[11] The fact that the best yield of **2** was obtained when using 4 equiv. of manganese(III) acetate could therefore be explained by two radical generation and oxidation sequences.

Trichloroamide **9** underwent a similar cyclisation, to form diene **10** in 94% yield, when treated with 0.5 equiv. of copper(I) chloride/bipyridine (Scheme 3). Both the formation of **2** and **10** was expected to require only a catalytic amount of the copper(I) complex as the copper(II), formed on generation of **4**, is reduced back to copper(I) on reaction with tertiary radical **5**. However, when **9** was treated with 0.25 equiv. of copper(I) chloride/bipyridine the yield of **10** decreased to 84% and a small amount of starting material (4%) was recovered. It is not clear, therefore, why more than 0.25 equiv. of the copper(I) complex is required although the formation of **10** (and **2**) requires the loss of HCl which could disrupt the catalytic cycle.

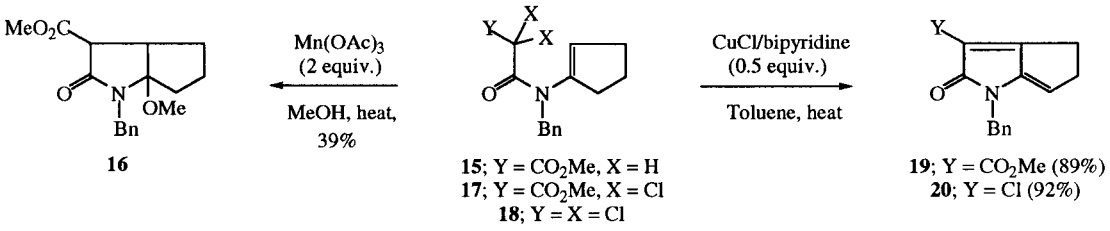
Reaction of related β-amido esters to **1**, showed that the efficiency of the manganese(III) promoted cyclisation was affected by the nature of the *N*-protecting group. For example, when the corresponding *N*-butyl (rather than *N*-benzyl) enamide was reacted, the yield of the diene increased from 38 to 52%. Of particular note, however, was the reaction of the *N*-allyl derivative **11**, which has the option to undergo ring closure by either a 5-*endo* or 5-*exo* pathway (by attack at the enamide or *N*-allyl double bond, respectively) (Scheme 4). Reaction of **11** with 4 equiv. of manganese(III) acetate, unexpectedly, produced the oxindole **12** in 17% yield. This yield could be increased to 46% when 8 equiv. of manganese(III) acetate were added portionwise to **11** over 8 h. It seems likely therefore, that 5-*endo* cyclisation leads to an intermediate diene (of type **2**) and the presence of



Scheme 3.



Scheme 4.



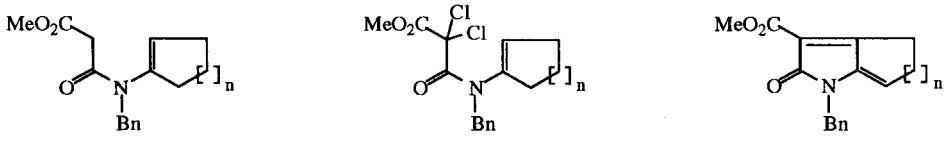
Scheme 5.

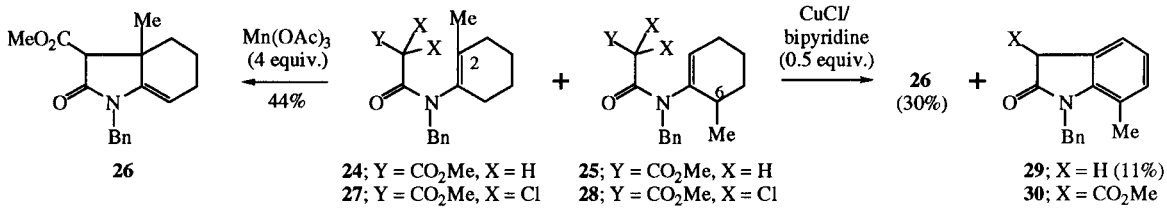
an *N*-allyl group encourages further oxidation to give an oxindole, although the reason for this is unclear. The formation of oxindole **12** contrasts with the efficient formation of bicyclic diene **14** from reaction of *N*-allyl trichloroamide **13** with copper(I) chloride/bipyridine. The presence of an *N*-benzyl or *N*-allyl protecting group clearly has little influence on this copper(I)-mediated cyclisation.

A marked difference in reaction products was also observed on cyclisation of enamides bearing a cyclopentene ring (Scheme 5). On portionwise addition of 2 equiv. of manganese(III) acetate (over 8 h) to **15**, the methoxy derivative **16** was isolated in an optimum yield of 39% (as a single diastereomer from the NMR spectra). Thus the intermediate *N*-acyliminium ion (of type **6**) reacts with methanol before deprotonation can take place. The deprotonation may be slower than for the 6-ring system because of the greater strain associated with a 5,5- rather than a 5,6-bicyclic ring. In contrast, when the related dichloroamide **17** or trichloroamide **18** were reacted with 0.5 equiv. of copper(I) chloride/bipyridine, the bicyclic dienes **19** and **20** were formed, respectively. The presence of a non-nucleophilic solvent (i.e. toluene) therefore allows deprotonation of the *N*-acyliminium ion to form an alkene, which is then converted to diene **19** or **20** on loss of HCl.

Surprisingly, when manganese(III) acetate was reacted with β-amidoesters **21ab**, bearing cycloheptene or cyclooctene rings, respectively, no cyclised products were isolated. A similar result was also obtained when using the corresponding *N*-butyl precursors. In contrast, the copper(I)-mediated cyclisation of dichloroesters **22a** and **22b** proceeded as expected, and the bicyclic dienes **23a** and **23b** were isolated in 86 and 90% yield, respectively.

The cyclisation of cyclohexene precursors, bearing a methyl substituent, also produced an interesting contrast in reagent reactivity. When a 1:1.5 mixture of (inseparable) alkene isomers **24** and **25** was heated with 4 equiv. of manganese(III) acetate, bicyclic alkene **26** was isolated in 44% yield (Scheme 6). This is presumably derived from cyclisation of the trisubstituted alkene **24** and no product derived from cyclisation of **25** was recovered. This could be explained by isomerisation of **25**, to give the more stable (tetrasubstituted) alkene **24**, under the acid reaction conditions. Indeed, when a 1:1.5 mixture of **24** and **25** was heated

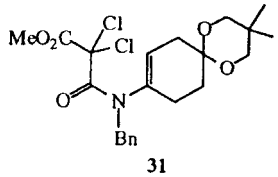




Scheme 6.

in methanol containing acetic acid (for 8 h), the alkene ratio changed to 1.2:1 in favour of **24**. In contrast, reaction of an inseparable 2.6:1 mixture of 2- and 6-methylcyclohexenyl dichlorides **27** and **28**, with 0.5 equiv. of copper(I) chloride/bipyridine, gave a mixture of oxindole **29** and alkene **26**. It is believed that alkene **26** is formed from cyclisation of **27**, following a similar mechanism to the related manganese(III) reaction. The presence of an α-hydrogen atom in **26** presumably results from chlorine-atom abstraction followed by reaction with an (unidentified[§]) hydrogen atom donor. Oxindole **29** could be formed on hydrolysis and decarboxylation (during silica gel chromatography) of the corresponding α-methyl ester **30** as related esters are known to be hydrolytically unstable.[12] Therefore, introduction of a 6-methyl substituent in the enamide precursor, leads to further oxidation of an intermediate diene (of type **2**) to give an oxindole, while the introduction of a 2-methyl substituent effectively prevents any further oxidation of alkene **26**.

Oxindole products were also obtained from enamide precursors with different substituents at alternative positions of the ring. For example, reaction of copper(I) chloride/bipyridine with acetal **31** produced oxindole **32** (in 35% yield), while carbamate **33** gave oxindoles **34** and **35** (in 15 and 19% yield), together with diene **36** (in 59% yield). The introduction of these functional groups on the cyclohexene ring clearly makes the intermediate diene more susceptible to oxidation. However, further oxidation can be prevented when using enamides with a more rigid ring system. Hence, reaction of decalene **37**, prepared from a mixture of *cis*- and *trans*-decalone, produced only diene **38** in 79% yield (as a single (ring junction) isomer from the NMR spectra) under the same reaction conditions; the ring strain associated with the tricyclic ring of **38** presumably hinders further oxidation.



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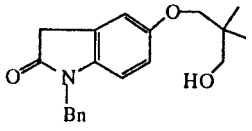

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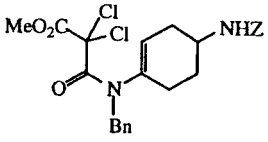

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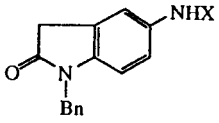
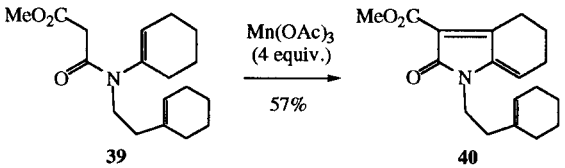
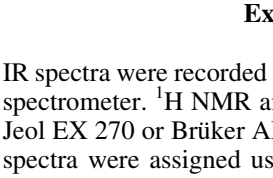


34; X = Z
35; X = H



39 40



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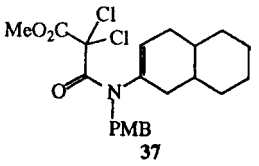

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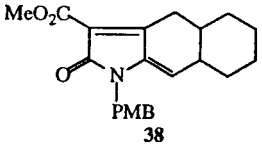

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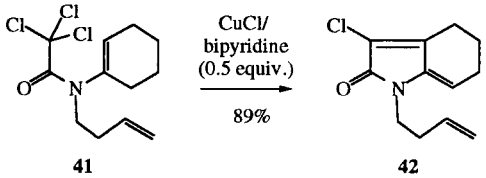
This work has demonstrated that the 5-*endo-trig* cyclisation of enamides can be initiated using either manganese(III) acetate or copper(I) chloride/bipyridine. Whereas a variety of precursors could be efficiently cyclised using copper(I) chloride/bipyridine, reactions using manganese(III) acetate were less predictable and proved to be very sensitive to the nature of the substrate. However, both of these methods provide a quick, easy and mild approach to a variety of functionalised pyrrolidinones in one-pot transformations. In all cases, the reactions are presumed to proceed via oxidation of a tertiary radical to an *N*-acyliminium ion (of type **5** and **6**, respectively). However, attempts to trap these intermediates by reaction with a second double bond (in a tandem cyclisation process[13]) were unsuccessful. Hence, for example, reaction of **39** with manganese(III) acetate produced diene **40**, while reaction of **41** with copper(I)/bipyridine produced diene **42** (Scheme 7). The rate of radical oxidation and cation deprotonation is therefore faster than (radical or cationic) cyclisation onto electron-rich double bonds.

Experimental

IR spectra were recorded on an ATI Mattison Genesis FT IR spectrometer. ^{1}H NMR and ^{13}C spectra were recorded on a Jeol EX 270 or Brüker AMX 500 spectrometer. The carbon spectra were assigned using DEPT experiments. Coupling constants (*J*) were recorded in Hertz to the nearest 0.5 Hz. Mass spectra were recorded on a Fisons Instruments VG Analytical Autospec Spectrometer system. Thin layer chromatography (TLC) was performed on Merck aluminium-backed silica gel plates. The Chemical Analytical Services Unit, University of Newcastle performed microanalyses using a Carlo Erba 1106 Elemental Analyser. Compounds were visualised under a UV lamp, using alkaline potassium



41 42

Scheme 7.

[§] When the reaction was carried out in d_8-toluene no deuterium was incorporated into **26** (or **29**).

permanganate solution and/or iodine. Column chromatography was performed using silica gel (Matrix Silica 60, 70–200 μm Fisons or ICN flash silica 60, 32–63 μm). Petroleum ether refers to the fraction with b.p. 40–60°C. Toluene was dried over calcium hydride, distilled, and stored over 3 Å molecular sieves under a nitrogen atmosphere. Enamide precursors for manganese (**11**, **15**, **24/25**, **39**) and copper (**9**, **13**, **17**, **18**, **22ab**, **27/28**, **31**, **33**, **37**, **41**) mediated cyclisations were prepared using the general procedures; the preparation of **1** and **3** are shown as representative examples.

General procedure for enamide formation

To a stirred solution of the ketone (2.55–8.32 mmol) in benzene or toluene (50–100 cm^3) was added the appropriate amine (2.55–8.32 mmol) and the solution was heated at reflux under Dean–Stark conditions until no starting material could be detected by TLC analysis (typically 7–10 h). The solution was then cooled to 0°C and methyl malonyl chloride (2.55–8.32 mmol) added dropwise, followed by the slow addition of *N*,*N*-diethylaniline (2.55–8.32 mmol). The mixture was allowed to warm to room temperature and left to stir for 2 h. Water was then added and the organic phase separated and washed with more water, brine, dried ($MgSO_4$) and evaporated in vacuo to afford crude product which was purified using column chromatography (silica) to give the enamides (24–76%), usually as oils.

Methyl [*N*-benzyl-*N*-(cyclohex-1-enyl)carbamoyl]ethanoate 1. Cyclohexanone (0.52 g, 0.55 cm^3, 5.30 mmol) was reacted with benzylamine (0.57 g, 0.58 cm^3, 5.30 mmol), methyl malonyl chloride (0.72 g, 0.57 cm^3, 5.30 mmol) and *N,N*-diethylaniline (0.79 g, 0.86 cm^3, 5.30 mmol) in benzene (100 cm^3) following the general procedure. Work-up afforded crude product which was purified using column chromatography (silica; petroleum ether–diethyl ether, 1:3) to afford **1** (0.85 g, 56%) as a yellow oil; R_f 0.24 (petroleum ether–diethyl ether, 1:3); ν_{max} (thin film) 2929 (s), 2858 (s), 1743 (s), 1653 (s), 1495 (w), 1437 (m), 1406 (m), 1329 (w), 1154 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.26-7.17 (5H, m, aromatics), 5.40 (1H, s, NC=C*H*), 4.60 (2H, s, NCH_2), 3.69 (3H, s, CO_2CH_3), 3.43 (2H, s, CH_2CO), 1.95 (4H, br s, CH_2CH and CH_2CNCH_2), 1.65–1.45 (4H, m, CH_2CH_2); δ_C (67.5 MHz, $CDCl_3$) 168.3, 165.2 (CO_2CH_3 and NCO), 137.8, 137.3 (NC=CH and CH_2C=CH), 129.1, 128.4, 128.1, 127.0 (CH=CH and NC=CH), 52.1 (CO_2CH_3), 49.3 (CH_2CO), 40.9 (NCH_2), 27.7, 24.5 (CH_2CH and CH_2CNCH_2), 22.4, 21.1 (CH_2CH_2); *m/z* (CI, NH_3) 288 ($M+H^+$, 100%), 230 (6), 198 (21), 188 (12), 108 (10), 98 (16), 91 (8), 35 (56); Found: $M+H^+$, 288.1595. $C_{17}H_{21}NO_3$ requires for $M+H^+$, 288.1599.

General procedure for manganese(III) acetate mediated cyclisation

To a stirred solution of the alkene (0.26–0.84 mmol) in methanol (5–15 cm^3) under nitrogen was added a suspension of $Mn(OAc)_3{\cdot}2H_2O$ (2–8 equiv.) in methanol (10–20 cm^3), in one portion or dropwise. The mixture was heated at reflux until no starting material could be detected by TLC analysis. The solvent was then removed under reduced pressure and ethyl acetate (15 cm^3) and water (15 cm^3) was added to the crude product. The organic layer was separated, washed with water, brine, dried ($MgSO_4$) and then evaporated under reduced pressure. The resultant residue was purified by flash column chromatography (silica) to afford cyclic products.

***N*-Benzyl-3-methoxycarbonyl-1,4,5,6-tetrahydro-indol-2-one 2**; 38%; colourless oil; R_f 0.28 (diethyl ether); ν_{max} (thin film) 3009 (w), 2929 (w), 1707 (s), 1650 (s), 1609 (w), 1437 (m), 1382 (m), 1138 (m) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.27–7.14 (5H, m, aromatics), 5.75 (1H, t, *J*=5 Hz, NC=C*H*), 4.72 (2H, s, NCH_2) 3.82 (3H, s, CO_2CH_3), 2.97 (2H, t, *J*=6.5 Hz, CH_2C=C), 2.29–2.20 (2H, m, CH_2CH=C), 1.67 (2H, quin., *J*=6.5 Hz, $CH_2CH_2CH_2$); δ_C (67.5 MHz, $CDCl_3$) 163.4, 156.8 (CO_2CH_3 and NCO), 155.7 (C=CCO_2CH_3), 138.0, 137.0 (NC=CH and C=CH), 128.6, 127.4, 127.3 (CH=CH and C=CCO_2CH_3), 116.5 (NC=CH), 51.8 (CO_2CH_3), 42.8 (NCH_2), 29.7, 24.4, 22.6 (CH_2); *m/z* (CI, NH_3) 284 ($M+H^+$, 100%), 251 (23), 224 (18), 195 (10), 167 (17), 149 (16); Found: $M+H^+$, 284.1287. $C_{17}H_{17}NO_3$ requires for $M+H^+$, 284.1287.

Methyl *N*-allyl-3-hydroxy-2-oxo-3-indolinecarboxylate 12; 46%; colourless oil; R_f 0.31 (petroleum ether–diethyl ether, 1:2); ν_{max} (thin film) 2933 (m), 1754 (s), 1711 (s), 1454 (w), 1405 (m) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.46–7.21 (3H, m, aromatics), 7.07–7.01 (1H, m, aromatics), 5.83–5.71 (1H, m, CH=CH_2), 5.35–5.18 (2H, m, CH=CH_2), 4.40–4.31 (1H, ddt, *J*=15.5, 4.5, 2 Hz, NCH_2), 4.06–3.96 (1H, ddt, *J*=15.5, 4.5, 2 Hz, NCH_2), 3.41 (3H, s, CO_2CH_3), [O*H* not observed]; δ_C (67.5 MHz, $CDCl_3$) 172.7, 170.3 (CO_2CH_3 and NCO), 143.8 (NC=CH), 130.6 (CH_2CH=CH_2), 130.5, 126.7, 123.9 (CH=CH), 118.4 (CH=CH_2), 109.8 (COH), 53.6 (CO_2CH_3), 42.5 (NCH_2); *m/z* (CI, NH_3) 265 ($M+NH_4^+$, 100%), 248 ($M+H^+$, 16), 191 (6), 174 (17); Found: $M+H^+$, 248.0929. $C_{13}H_{13}NO_4$ requires for $M+H^+$, 248.0923.

Methyl *N*-benzyl-6a-methoxy-2-oxo-octapenta[a,b]pyrrole-3-carboxylate 16; 39%; colourless oil; R_f 0.53 (petroleum ether–ethyl acetate, 1:1); ν_{max} (thin film) 2927 (m), 1739 (s), 1696 (s), 1432 (w), 1403 (m) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.38–7.21 (5H, m, aromatics), 4.70 (1H, d, *J*=15 Hz, NCH_2), 4.16 (1H, d, *J*=15 Hz, NCH_2), 3.81 (3H, s, CO_2CH_3), 3.20 (1H, d, *J*=5 Hz, CHCO), 3.06 (3H, s, $NCOCH_3$), 2.99–2.93 (1H, m, CHCHCO), 2.09–2.04 (2H, m, CH_2COCH_3), 1.74–1.44 (4H, m, CH_2CH_2); δ_C (67.5 MHz, $CDCl_3$) 170.2, 169.9 (CO_2CH_3 and NCO), 137.4 (C=CH), 128.4, 128.0, 127.9, 127.5, 127.3 (CH=CH), 105.0 ($COCH_3$), 52.8 ($COCH_3$), 50.8 (CO_2CH_3), 45.6 (CHCO), 43.5 (NCH_2), 41.4 (CHCHCO), 38.1 (CH_2COCH_3), 33.6, 21.9 (CH_2CH_2); *m/z* (CI, NH_3) 304 ($M+H^+$, 83%), 272 (100), 214 (7); Found: $M+H^+$, 304.1544. $C_{17}H_{21}NO_4$ requires for $M+H^+$, 304.1549.

Methyl *N*-benzyl-3a-methyl-2-oxo-2,3,3a,4,5,6-hexahydro-indole-3-carboxylate 26; 44%; colourless oil; R_f 0.23 (petroleum ether–diethyl ether, 1:1); ν_{max} (thin film) 2925 (m), 1758 (s), 1693 (s), 1435 (m), 1403 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.35–7.21 (5H, m, aromatics), 4.79 (1H, t, *J*=3.5 Hz, NC=C*H*), 4.70 (2H, s, NCH_2), 3.72 (3H, s, CO_2CH_3), 3.30 (1H, s, CHCO), 2.08–1.73 (6H, m, CH_2CH_2), 1.28 (3H, s, CCH_3); δ_C (67.5 MHz, $CDCl_3$)

173.0, 168.7 (CO_2CH_3 and N*C*O), 143.4 (N*C*=CH), 138.2 (CH_2C=CH), 128.7, 128.6, 128.5, 128.4, 127.3, 127.1 (*C*H=CH and NC=*C*H), 59.2 (*C*HCO), 52.1 (CO_2CH_3), 43.4 (NCH_2), 40.2 (CCH_3), 30.2 (CH_2CH), 22.4 (CH_2CCH_3), 21.6 ($CH_2CH_2CH_2$), 15.1 (CCH_3); *m/z* (CI, NH_3) 317 ($M+NH_4^+$, 45%), 300 ($M+H^+$, 100); Found: $M+H^+$, 300.1602. $C_{18}H_{21}NO_3$ requires for $M+H^+$, 300.1599.

Methyl *N*-[2-(1-cyclohex-1-enyl)ethyl]-2-oxo-2,4,5,6-tetrahydro-indole-3-carboxylate 40; 57%; colourless oil; R_f 0.23 (petroleum ether–diethyl ether, 1:2); ν_{max} (thin film) 2932 (m), 1736 (s), 1709 (s), 1440 (m), 1402 (m) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 5.97 (1H, t, *J*=5 Hz, NC=C*H*), 5.46 (1H, s, C=C*H*), 3.93 (3H, s, CO_2CH_3), 3.70 (2H, t, *J*=6.5 Hz, NCH_2), 3.10 (2H, t, *J*=6.5 Hz, CH_2C=C), 2.53–2.47 (1H, m, CH_2CH=CN), 2.23 (2H, t, *J*=7.5 Hz, NCH_2CH_2), 1.98–1.89 (6H, m, CH_2CCH_2, CH_2CH and CH_2CH_2C=C), 1.69–1.58 (4H, m, CH_2CH_2); δ_C (67.5 MHz, $CDCl_3$) 165.5, 163.4 (CO_2CH_3 and N*C*O), 155.1 (C=*C*CO_2CH_3), 138.2 (N*C*=CH), 123.4 (*C*=CCO_2CH_3), 116.9 (CH_2C=CH), 115.2 (NC=*C*H), 51.6 (CO_2CH_3), 38.0 (NCH_2), 36.6 (CH_2C=C), 28.3, 25.2, 24.4 (CH_2C=CH and $CHCH_2$), 22.8, 22.1 ($CH_2CH_2CH_2$); *m/z* (CI, NH_3) 296 ($M+NH_4^+$, 23%), 279 ($M+H^+$,100); Found: $M+H^+$, 279.1604. $C_{15}H_{23}NO_3$ requires for $M+H^+$, 279.1606.

General procedure for chlorination of alkenes

To a stirred solution of the alkene (0.52–1.95 mmol) in dry tetrahydrofuran (10–15 cm^3) at 0°C, under an atmosphere of nitrogen, was added sodium hydride (1.15–4.29 mmol). The solution was allowed to stir for 1 h after which *N*-chlorosuccinimide (1.15–4.29 mmol) was added, the solution allowed to warm to room temperature and stirred for a further 2 h. The solvent was then evaporated under reduced pressure and water (10 cm^3) and ethyl acetate (10 cm^3) were added. The organic phase was separated, washed with more water, brine, dried ($MgSO_4$) and then evaporated under reduced pressure to afford crude product which was purified using column chromatography (silica) to afford the chlorinated products (69–84%), usually as oils.

Methyl [*N*-benzyl-*N*-(cyclohex-1-enyl)carbamoyl]-2,2-dichloroethanoate 3. Enamide **1** (150 mg, 0.52 mmol), sodium hydride (28 mg, 47 mg of a 60% dispersion in mineral oil, 1.15 mmol) and *N*-chlorosuccinimide (154 mg, 1.15 mmol) were reacted together in dry tetrahydrofuran (8 cm^3) following the general procedure. Column chromatography (silica; petroleum ether–diethyl ether, 1:1) afforded the desired product **3** (146 mg, 79%) as a colourless oil; R_f 0.45 (petroleum ether–diethyl ether, 1:1); ν_{max} (thin film) 2935 (s), 1767 (s), 1744 (m), 1679 (s), 1452 (m), 1437 (m), 1393 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.32–7.21 (5H, m, aromatics), 5.40 (1H, br s, NC=C*H*), 5.05 (1H, d, *J*=14 Hz, NC*H*), 4.25 (1H, d, *J*=14 Hz, NC*H*), 3.84 (3H, s, CO_2CH_3), 2.17–1.83 (4H, m, CH_2CH and CH_2CCH), 1.54–1.25 (4H, m, CH_2CH_2); δ_C (67.5 MHz, $CDCl_3$) 164.1, 161.5 (CO_2CH_3 and N*C*O), 136.3, 135.9 (N*C*=CH and *C*=CH), 131.4, 128.4, 128.3, 127.5 (*C*H=CH and NC=*C*H), 80.5 (CCl_2), 54.4 (CO_2CH_3), 51.6 (NCH_2), 27.2, 24.6 (CH_2CH and CH_2CCH), 22.2, 20.9 (CH_2CH_2); *m/z* (CI, NH_3) 358 ($^{35,37}M+H^+$, 57%), 356 ($^{35}M+H^+$, 89), 320 (69), 286 (100), 271 (51), 254 (11), 226 (19), 186 (24), 108 (7), 91 (20); Found: $^{35}M+H^+$, 356.0814. $C_{17}H_{19}Cl_2NO_3$ requires for $^{35}M+H^+$, 356.0820.

General procedure for copper(I) chloride mediated cyclisation

To a stirred solution of the alkene (0.22 mmol) and copper(I) chloride (0.11 mmol) in dry degassed toluene (1.5 cm^3) under an atmosphere of nitrogen was added a solution of 2,2′-bipyridine (0.11 mmol) in toluene (0.5 cm^3). The mixture was heated at reflux until no starting material could be detected by TLC analysis. The solvent was removed under reduced pressure and the residue purified by column chromatography (silica) to afford cyclic product(s), typically as oils.

Copper(I) mediated cyclisation of *N*-benzyl-2,2,2-trichloro-*N*-(cyclohex-1-enyl)ethanamide 3. Enamide **3** (73 mg, 0.22 mmol), copper(I) chloride (6 mg, 0.06 mmol) and 2,2′-bipyridine (9 mg, 0.06 mmol) were reacted together in dry toluene (2 cm^3) following the general procedure. Column chromatography (silica; petroleum ether–diethyl ether, 3:1) afforded **2** (47 mg, 84%) as a pale yellow oil. The spectral data for **2** was identical to that reported earlier.

***N*-Benzyl-3-chloro-1,4,5,6-tetrahydro-indol-2-one 10**; 94%; pale yellow oil; R_f 0.32 (petroleum ether–diethyl ether, 3:1); (Found: C, 64.06; H, 5.54; N, 4.96. $C_{15}H_{14}ClNO$ requires C, 64.31; H, 5.83; N, 5.09%); ν_{max} (thin film) 2912 (w), 1714 (s), 1692 (m), 1438 (w), 1399 (w), 1246 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.65–7.22 (5H, m, aromatics), 5.59 (1H, t, *J*=4.5 Hz, NC=C*H*), 4.80 (2H, s, NCH_2), 2.62 (2H, t, *J*=6.5 Hz, CH_2C=C), 2.31–2.26 (2H, m, CH_2CH=C), 1.81 (2H, q, *J*=6.5 Hz, $CH_2CH_2CH_2$); δ_C (67.5 MHz, $CDCl_3$) 164.8 (N*C*O), 137.1, 137.0 (2× *C*=CH and N*C*=CH), 128.7, 127.5, 127.2 (*C*H=CH and Cl*C*=C), 111.7 (NC=*C*H), 43.5 (NCH_2), 24.3, 22.6, 22.3 (CH_2CH_2); *m/z* (CI, NH_3) 262 ($^{37}M+H^+$, 34%), 260 ($^{35}M+H^+$, 100), 226 (11), 170 (9); Found: $^{35}M+H^+$, 260.0837. $C_{15}H_{14}ClNO$ requires for $^{35}M+H^+$, 260.0842.

***N*-Allyl-3-chloro-1,4,5,6-tetrahydro-indol-2-one 14**; 91%; colourless oil; R_f 0.36 (petroleum ether–diethyl ether, 3:1); ν_{max} (thin film) 2929 (w), 1705 (s), 1656 (m), 1437 (w), 1411 (w), 1317 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 5.85–5.71 (1H, m, C*H*=CH_2), 5.68 (1H, t, *J*=4 Hz, NC=C*H*), 5.17–5.13 (2H, m, CH=CH_2), 4.25 (2H, s, NCH_2), 2.63 (2H, t, *J*=6.5 Hz, CH_2C=C), 2.39–2.33 (2H, m, CH_2CHC), 1.83 (2H, q, *J*=6.5 Hz, $CH_2CH_2CH_2$); δ_C (67.5 MHz, $CDCl_3$) 164.4 (N*C*O), 139.7, 137.2 (Cl*C*=*C* and N*C*=CH), 132.9 (*C*H=CH_2), 119.3 (Cl*C*=C), 116.8 (CH=*C*H_2), 111.5 (NC=*C*H), 42.2 (NCH_2), 24.3, 22.6, 22.3 (CH_2CH_2); *m/z* (CI, NH_3) 212 ($^{37}M+H^+$, 32%), 210 ($^{35}M+H^+$, 100), 176 (9); Found: $^{35}M+H^+$, 210.0684. $C_{11}H_{12}ClNO$ requires for $^{35}M+H^+$, 210.0686.

Methyl *N*-benzyl-2-oxo-1,2,4,5-tetrahydro-cyclopenta[a,b]-pyrrole-3-carboxylate 19; 89%; colourless oil; R_f 0.18 (petroleum ether–diethyl ether, 1:4); (Found: C, 70.31; H, 5.68; N, 4.99. $C_{16}H_{15}NO_3$ requires C, 70.11; H, 5.61; N,

5.20%); ν_{max} (thin film) 2951 (w), 1739 (s), 1711 (s), 1648 (m), 1437 (m), 1351 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.34–7.23 (5H, m, aromatics), 5.76 (1H, t, J=3 Hz, NC=C*H*), 4.82 (2H, s, NCH_2), 3.87 (3H, s, CO_2CH_3), 3.04–2.98 (2H, m, CH_2CH_2), 2.90–2.85 (2H, m, CH_2CH_2); δ_C (67.5 MHz, $CDCl_3$) 169.9, 163.0 (CO_2CH_3 and NCO), 144.4 (C=CCO_2CH_3), 138.9, 136.6 (NC=CH and C=CH), 128.7, 127.9, 127.7 (CH=CH), 120.3 (NC=CH), 112.5 (C=CCO_2CH_3), 51.7 (CO_2CH_3), 44.6 (NCH_2), 35.8, 26.4 (CH_2CH_2); *m/z* (CI, NH_3) 269 ($M+H^+$, 34%), 237 (17), 208 (27), 181 (44), 91 (100); Found: $M+H^+$, 269.1059. $C_{16}H_{15}NO_3$ requires for $M+H^+$, 269.1052.

***N*-Benzyl-3-chloro-4,5-dihydro-cyclopenta[a,b]pyrrol-2-one 20**; 92%; colourless oil; R_f 0.29 (petroleum ether–diethyl ether, 4:1); ν_{max} (thin film) 2921 (m), 1711 (s), 1650 (m), 1454 (w), 1436 (w), 1402 (w), 1327 (w), 1246 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.34–7.23 (5H, m, aromatics), 5.47 (1H, t, J=3 Hz, NC=C*H*), 4.82 (2H, s, NCH_2), 2.83–2.74 (4H, m, CH_2CH_2); δ_C (67.5 MHz, $CDCl_3$) 169.2 (NCO), 153.6 (ClC=*C*), 143.3 (NC=CH), 136.5 (*C*=CH), 128.6, 127.7, 127.6 (CH=CH), 114.4 (NC=*C*H), 45.3 (NCH_2), 34.6, 23.2 (CH_2CH_2); *m/z* (CI, NH_3) 248 ($^{37}M+H^+$, 34%), 246 ($^{35}M+H^+$, 100), 212 (100), 91 (9); Found: $^{35}M+H^+$, 246.0683. $C_{14}H_{12}ClNO$ requires for $^{35}M+H^+$, 246.0685.

Methyl *N*-benzyl-2-oxo-1,2,4,5,6,7-hexahydro-cyclohepta[a,b]pyrrole-3-carboxylate 23a; 86%; pale yellow oil; R_f 0.32 (petroleum ether–diethyl ether, 1:4); ν_{max} (thin film) 2950 (w), 1736 (s), 1711 (s), 1648 (m), 1437 (m), 1399 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.33–7.20 (5H, m, aromatics), 5.88 (1H, t, J=6 Hz, NC=C*H*), 4.85 (2H, s, NCH_2), 3.90 (3H, s, CO_2CH_3), 3.16 (2H, m, CH_2C=C), 2.48–2.42 (2H, m, CH_2CH), 1.81–1.77 (4H, m, $CH_2CH_2CH_2$); δ_C (67.5 MHz, $CDCl_3$) 165.2, 163.0 (CO_2CH_3 and NCO), 158.9 (*C*=CCO_2CH_3), 138.9, 137.1 (NC=CH and *C*=CH), 128.2, 127.3, 127.0 (CH=CH), 122.3 (NC=*C*H), 117.0 (C=*C*CO_2CH_3), 52.0 (CO_2CH_3), 42.8 (NCH_2), 28.9, 28.7 (CH_2C=C and CH_2CH), 26.7, 24.1 ($CH_2CH_2CH_2$); *m/z* (CI, NH_3) 298 ($M+H^+$, 100%), 256 (9), 242 (15), 91 (10); Found: $M+H^+$, 298.1442. $C_{18}H_{19}NO_3$ requires for $M+H^+$, 298.1443.

Methyl *N*-benzyl-2-oxo-2,4,5,6,7,8-hexahydro-cycloocta-[a,b]pyrrole-3-carboxylate 23b; 90%; colourless oil; R_f 0.43 (petroleum ether–diethyl ether, 1:4); ν_{max} (thin film) 2931 (w), 1723 (s), 1694 (m), 1496 (m), 1437 (m), 1382 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.33–7.20 (5H, m, aromatics), 5.65 (1H, t, J=9 Hz, NC=C*H*), 4.87 (2H, s, NCH_2), 3.90 (3H, s, CO_2CH_3), 3.23 (2H, t, J=7 Hz, CH_2C=C), 2.58 (2H, quin., J=7 Hz, CH_2CH), 1.79–1.72 (2H, m, C=CCH_2CH_2 or C=$CHCH_2CH_2$), 1.56–1.49 (2H, m, C=CCH_2CH_2 or C=$CHCH_2CH_2$), 1.43–1.38 (2H, m, CH_2CH_2); δ_C (67.5 MHz, $CDCl_3$) 165.6, 163.7 (CO_2CH_3 and NCO), 156.9 (*C*=CCO_2CH_3), 141.7, 136.9 (NC=CH and *C*=CH), 128.6, 127.3, 126.8 (CH=CH), 122.2 (NC=*C*H), 116.7 (C=*C*CO_2CH_3), 52.0 (CO_2CH_3), 42.6 (NCH_2), 26.5, 25.3 (CH_2C=C and CH_2CH), 24.9, 24.5 (C=CCH_2CH_2 and C=$CHCH_2CH_2$), 21.2 (CH_2CH_2); *m/z* (CI, NH_3) 312 ($M+H^+$, 100%); Found: $M+H^+$, 312.1597. $C_{19}H_{21}NO_3$ requires for $M+H^+$, 312.1599.

Copper(I) mediated cyclisation of methyl [*N*-benzyl-*N*-(2-methyl-cyclohex-1-enyl)carbamoyl]-2,2-dichloroethanoate 27 and methyl [*N*-benzyl-*N*-(6-methyl-cyclohex-1-enyl)carbamoyl]-2,2-dichloroethanoate 28. A 2.6:1 mixture of enamides **27** and **28** (81 mg, 0.22 mmol), copper (I) chloride (10 mg, 0.11 mmol) and 2,2′-bipyridine (16 mg, 0.11 mmol) were reacted together in dry toluene (2 cm^3) following the general procedure. Column chromatography (silica; petroleum ether–diethyl ether, 1:2) afforded an inseparable mixture of **26** (20 mg, 30%) and ***N*-benzyl-7-methyl-1,3-dihydro-indol-2-one 29** (6 mg, 11%), as a colourless oil; R_f 0.43 (petroleum ether–diethyl ether, 1:2); ν_{max} (thin film) 2953 (w), 1710 (s), 1604 (s), 1471 (m), 1446 (w) cm^{-1}. **29**; δ_H (270 MHz, $CDCl_3$) 7.34–7.21 (5H, m, aromatics), 7.17–7.10 (3H, m, aromatics), 5.20 (2H, s, NCH_2Ph), 3.65 (2H, s, CH_2CON), 1.61 (3H, s, CCH_3); δ_C (67.5 MHz, $CDCl_3$, mixture with **26**) 176.0, 170.1, 169.2 (CO_2CH_3 and NCO), 142.3 (NC=CH), 137.8, 136.8, 136.0 (NC=CCH_3, NC=*C*CH_3 and *C*=CH), 128.8, 128.5, 127.1, 125.6, 125.0, 122.4, 122.3, 119.8 (CH=CH and NC=*C*H), 60.8 ($CHCO_2CH_3$), 52.1 (CO_2CH_3), 45.0, 44.8 (NCH_2), 40.1 (CCH_3), 35.6 (CH_2CON), 30.1, 22.5, 21.5 (CH_2CH_2), 18.6, 17.9 (CCH_3); *m/z* (CI, NH_3) 238 ($M+H^+$, 100%), 91 (17); Found: $M+H^+$, 238.1232. $C_{16}H_{15}NO$ requires for $M+H^+$, 238.1231.

***N*-Benzyl-5-(3-hydroxy-2,2-dimethylpropoxy)-1,3-dihydro-indol-2-one 32**; 35%; colourless oil; R_f 0.25 (petroleum ether–ethyl acetate, 1:2); ν_{max} (thin film) 3471 (s), 2957 (m), 1703 (s), 1694 (s), 1598 (m), 1493 (m), 1453 (w), 1366 (m) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.27–7.22 (5H, m, aromatics), 6.87 (1H, s, CH_2C=C*H*), 6.67 (1H, dd, J=8.5 Hz, 2.5, NCCHC*H*), 6.55 (1H, d, J=8.5 Hz, NCC*H*), 4.87 (2H, s, NCH_2), 3.68 (2H, s, $COCH_2$), 3.56 (OCH_2), 3.51 (2H, s, CH_2OH), 0.99 (6H, s, $C(CH_3)_2$); δ_C (67.5 MHz, $CDCl_3$) 174.0 (NCO), 155.3 ($CHCOCH_2$), 144.4 (NCCH), 135.9 (C=*C*H), 128.7 (CH=CH), 127.9 ($COCH_2CCH$), 127.5, 127.3 (CH=CH), 113.0, 112.6 (NCCHCH and NCCHCH), 109.3 ($COCH_2CCH$), 75.8 ($CHCOCH_2C$), 69.9 (CH_2OH), 43.8 (NCH_2), 36.2 ($COCH_2$), 36.1 (CCH_3), 22.5, 21.6 (CH_3); *m/z* (CI, NH_3) 326 ($M+H^+$, 100%), 308 (3), 239 (12), 91 (15); Found: $M+H^+$, 326.1764. $C_{20}H_{23}NO_3$ requires for $M+H^+$, 326.1758.

Copper(I) chloride mediated cyclisation of methyl *N*-[benzyl(4-{[(benzyloxy)carbonyl]amino}-*N*-cyclohex-1-enyl)carbamoyl]-2,2-dichloroethanoate 33. To a stirred solution of dichloride **33** (111 mg, 0.22 mmol) and copper(I) chloride (10 mg, 0.11 mmol) in dry degassed toluene (1.5 cm^3) under an atmosphere of nitrogen was added a solution of 2,2′-bipyridine (16 mg, 0.11 mmol) in toluene (0.5 cm^3). The mixture was heated at reflux until no starting material could be detected by TLC analysis. The solvent was removed under reduced pressure and the residue purified by column chromatography (silica; petroleum ether–diethyl ether, 2:1), which afforded **34** (16 mg, 19%), **35** (7 mg, 15%) and **36** (56 mg, 59%) as colourless oils.

Benzyl *N*-benzyl-2-oxo-2,3-dihydro-indol-5-yl carbamate 34; R_f 0.11 (petroleum ether–diethyl ether, 2:1); ν_{max} (thin film) 2920 (w), 1711 (m), 1675 (s), 1609 (m),

1493 (m), 1452 (m), 1366 (w), 1358 (m) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.28–7.22 (5H, m, aromatics), 7.03 (1H, m, $COCH_2CCH$), 6.60 (2H, m, NCC*H* and NCCHC*H*), 5.16 (2H, s, OCH_2), 4.87 (2H, s, NCH_2), 3.58 (2H, s, $COCH_2$); δ_C (67.5 MHz, $CDCl_3$) 174.8 (N*C*O), 153.6 (NCO_2CH_2), 144.5, 140.5 (N*C*CH and *C*NCO_2), 136.0, 135.7 (C=*C*H), 128.8, 128.6, 128.3, 128.1, 127.6, 127.3 (*C*H=CH), 125.3 ($COCH_2CCH$), 118.7, 116.8 (NC*C*HCH and NCCH*C*H), 109.1 ($COCH_2CCH$), 67.1 (OCH_2), 43.8 (NCH_2), 36.0 ($COCH_2$); *m/z* (CI, NH_3) 373 ($M+H^+$, 45%), 256 (100), 239 (49), 108 (14), 91 (24); Found: $M+H^+$, 372.1468. $C_{23}H_{21}N_2O_3$ requires for $M+H^+$, 372.1471.

5-Amino-*N*-benzyl-1,3-dihydro-indol-2-one 35; R_f 0.27 (petroleum ether–diethyl ether, 2:1); ν_{max} (thin film) 1707 (m), 1614 (m), 1489 (m), 1466 (m), 1378 (w), 1358 (m) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.32–7.20 (7H, m, C*H*=CH), 7.17 (1H, t, *J*=7.5 Hz, C*H*=CH), 7.00 (1H, t, *J*=7.5 Hz, C*H*=CH), 6.72 (1H, d, *J*=7.5 Hz, C*H*=CH), 4.92 (2H, s, NCH_2), 3.63 (2H, s, $COCH_2$); δ_C (67.5 MHz, $CDCl_3$) 175.1 (N*C*O), 144.4 (N*C*CH), 135.8 (C=*C*H), 128.7, 127.8, 127.8, 127.6, 127.3, 124.4 (*C*H=CH), 124.3 ($COCH_2CCH$), 43.7 (NCH_2), 35.7 ($COCH_2$); *m/z* (CI, NH_3) 224 ($M+H^+$, 100%), 91 (9); Found: $M+H^+$, 224.1070. $C_{15}H_{14}NO$ requires for $M+H^+$, 224.1075.

Methyl *N*-benzyl-5-{[(benzyloxy)carbonyl]amino}-2-oxo-2,4,5,6-tetrahydro-indole-3-carboxylate 36; R_f 0.15 (diethyl ether); ν_{max} (thin film) 3323 (m), 2952 (m), 1734 (s), 1719 (s), 1655 (s), 1528 (w), 1453 (m), 1438 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.65–7.18 (10H, m, aromatics), 5.66 (1H, t, *J*=5 Hz, NC=C*H*), 5.08 (2H, s, OCH_2), 5.03 (1H, br s, N*H*), 4.82 (1H, d, *J*=15 Hz, NC*H*Ph), 4.74 (1H, d, *J*=15 Hz, NC*H*Ph), 4.10 (1H, br s, NC*H*), 3.87 (3H, s, CO_2CH_3), 3.46 (1H, dd, *J*=4, 18 Hz, NHCHC*H*), 2.89 (1H, dd, *J*=9.5, 18, NHCHC*H*), 2.68 (1H, dt, *J*=18, 5 Hz, NC=CHC*H*), 2.37–2.30 (1H, m, NC=CHC*H*); δ_C (67.5 MHz, $CDCl_3$) 165.8, 162.9 (CO_2CH_3 and N*C*O), 155.5, 152.7 (CO_2CH_2 and *C*=CCO_2CH_3), 137.8, 136.6, 136.1 (N*C*=CH and *C*=CH), 128.6, 128.3, 128.2, 127.6, 127.3 (*C*H=CH), 118.6 (C=*C*CO_2CH_3), 112.7 (NC=*C*H), 66.9 (OCH_2), 51.9 (CO_2CH_3), 46.9 (*C*HNH), 43.0 (NCH_2Ph), 31.1, 30.9 (CH_2); *m/z* (CI, NH_3) 433 ($M+H^+$, 9%), 224 (64), 152 (11), 108 (34), 91 (100); Found: $M+H^+$, 433.1757. $C_{25}H_{24}N_2O_5$ requires for $M+H^+$, 433.1763.

Methyl *N*-(4-methoxybenzyl)-2-oxo-2,4,4a,5,6,7,8,8a-octahydro-benzo-indole-3-carboxylate 38; 79%; colourless oil; R_f 0.29 (petroleum ether–diethyl ether, 1:2); ν_{max} (thin film) 2928 (m), 1735 (m), 1709 (s), 1685 (s), 1513 (m), 1440 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.15 (2H, d, *J*=9 Hz, C*H*=$COCH_3$), 6.82 (2H, d, *J*=9 Hz, C*H*=$COCH_3$), 5.82 (1H, br s, NC=C*H*), 4.72 (2H, s, NCH_2), 3.89 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 2.58–2.49 (4H, m, CH_2CH and 2× $CHCH_2$), 2.17–1.59 (8H, m, CH_2CH_2); δ_C (67.5 MHz, $CDCl_3$) 165.1, 163.3 (CO_2CH_3 and N*C*O), 158.8 (CH=*C*OCH_3), 138.6, 136.9, 133.5 (N*C*=CH, *C*=CH and *C*CO_2CH_3), 129.0, 128.8, 128.6 (*C*H=CH), 114.0 (NC=*C*H), 55.0, 53.4 ($COCH_3$ and CO_2CH_3), 42.3 (NCH_2), 36.3, 33.5 ($CHCH_2$), 28.9, 26.5, 20.6 (CH_2CH_2 and $CHCH_2$); *m/z* (CI, NH_3) 368 ($M+H^+$, 90%), 312 (100), 137 (24), 121 (35); Found: $M+H^+$, 368.1856. $C_{22}H_{25}NO_4$ requires for $M+H^+$, 368.1861.

***N*-(But-3-enyl)-3-chloro-1,4,5,6-tetrahydro-indol-2-one 42**; 89%; pale yellow oil; R_f 0.29 (petroleum ether–diethyl ether, 3:1); ν_{max} (thin film) 2937 (w), 1704 (s), 1654 (m), 1623 (w), 1439 (w), 1411 (w), 1341 (w) cm^{-1}; δ_H (270 MHz, $CDCl_3$) 5.81–5.72 (1H, m, CH_2CH=CH_2), 5.69 (1H, t, *J*=4.5 Hz, NC=C*H*), 5.10–5.02 (2H, m, CH_2CH=CH_2), 3.65 (2H, t, *J*=14.5 Hz, NCH_2), 2.62 (2H, t, *J*=6.5 Hz, CH_2C=C), 2.42–2.35 (4H, m, CH_2C=CH and NCH_2CH_2), 1.85 (2H, q, *J*=6.5 Hz, $CH_2CH_2CH_2$); δ_C (67.5 MHz, $CDCl_3$) 164.6 (N*C*O), 139.4 (ClC=*C*), 137.3 (N*C*=CH), 134.6 (*C*H=CH_2), 117.2 (CH=*C*H_2), 110.7 (NC=*C*H), 39.2 (NCH_2), 33.2 (NCH_2CH_2), 24.4, 22.7, 22.2 (CH_2CH_2); *m/z* (CI, NH_3) 226 ($^{37}M+H^+$, 32%), 224 ($^{35}M+H^+$, 100), 206 (5), 190 (16), 170 (12); Found: $^{35}M+H^+$, 224.0841. $C_{12}H_{14}ClNO$ requires for $^{35}M+H^+$, 224.0842.

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