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Intramolecular Dipolar Cycloaddition Reactions to Give Substituted Indoles – A Formal Synthesis of Deethylibophyllidine

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A four-step route to the tetracyclic ring system found in a number of indole alkaloids is described using stereoselective dipolar cycloaddition reactions of azomethine ylides. The ylides were derived from *N*-protected 2-butenylindole-3-carbaldehydes, which were prepared in three steps from 2-methylindole. Condensation of these aldehydes with a variety of alkylamino esters or amino acids or with *N*-methylhydroxylamine gave the required azomethine ylides or nitrone that undergo intramolecular cycloaddition onto the pendant, unactivated alkene. The cycloaddition sets up two new rings and up to three new stereocentres stereoselectively. After cycloaddition with *N*-allylglycine, *N*-deallylation provided the *N*-unsubstituted product and this constitutes a formal synthesis of the alkaloid deethylibophyllidine. The cycloaddition chemistry was also shown to be amenable as a route to the alkaloid ibophyllidine or epiibophyllidine, although the use of 2-(allylamino)butyric acid to prepare the azomethine ylide can favour competing iminium ion isomerisation and hydrolysis.

Introduction

The iboga plant is a member of the family Apocynaceae and contains a number of biologically active alkaloids.[1] The roots of *Tabernanthe iboga* have been used in African tribal initiation rites and confer hallucinogenic and stimulant properties. This plant contains the alkaloid ibogaine and a number of related alkaloids that have been used as medicinal agents, with current interest in their "anti-addictive" properties.[2] Within this family are the ibophyllidine group of alkaloids, including ibophyllidine, 20-epiibophyllidine and deethylibophyllidine (Figure 1).[3] The first synthesis of this type of alkaloid was reported by the group of Kuehne using a Diels–Alder approach.[4] Subsequent reports describe improved modifications of this chemistry.[5] A similar approach was reported by Das and co-workers, and by Kalaus and Szántay and co-workers.[6] A route using the Fischer indole synthesis has been reported by Bonjoch and co-workers,[7] who have also reported an alternative approach using a transannular cyclisation.[8] More recently Padwa and co-workers have described an approach to this type of alkaloid using a tandem Pummerer/Mannich cyclisation,[9] Banwell and Lupton have described a route to the tricyclic core,[10] and Kalaus and Szántay and co-workers have prepared 19-hydroxyibophyllidine.[11]

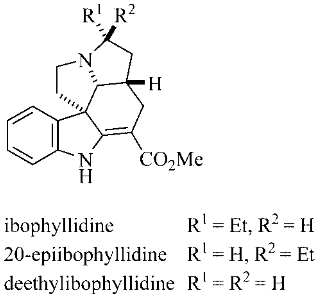

Figure 1. Ibophyllidine alkaloids.

One approach to polycyclic indole alkaloids involves the Pummerer cyclisation of sulfoxides, with the indole ring acting as the intramolecular nucleophile.[12] This was exploited in Bonjoch's synthesis, by addition of phenyl vinyl sulfoxide to the secondary amine **2** (R = H) to give the sulfoxide **1** (R = H) (Scheme 1).[7] The sulfoxide **1** (R = H) was then converted to deethylibophyllidine in 3 steps (Pummerer cyclisation, desulfurisation and photochemical 1,3-acyl shift). The amine **2** (R = H) was prepared in 6 steps from *O*-methyltyramine.[7] We wondered if amines such as **2** could be accessed from azomethine ylides **3**. These should be readily available by addition of an amine to an indole-3-carbaldehyde. The intramolecular cycloaddition of an azomethine ylide is an efficient method to prepare bicyclic amines and can be successful even with an unactivated alkene as the dipolarophile.[13,14] A convenient approach to such ylides involves the condensation of an aldehyde and an amino acid, with loss of CO_2 to give the desired ylide.[15]

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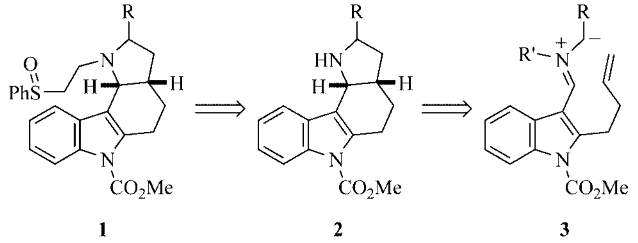
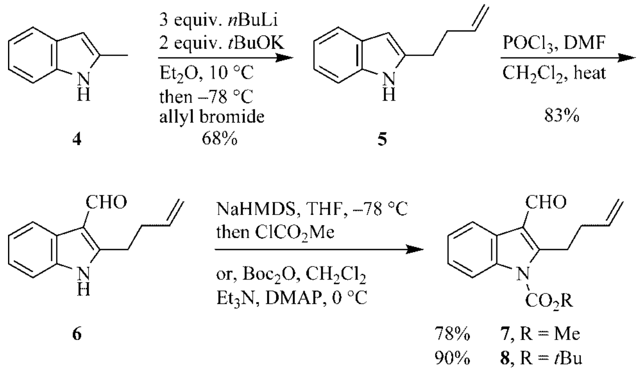
In fact, azomethine ylides have recently been generated from indole-3-carbaldehydes by this methodology, although these ylides subsequently undergo electrocyclic reaction onto the pendent 2-phenyl substituent.[16] In the absence of this phenyl group and in the presence of a dipolarophile, we reasoned that the ylides should undergo cycloaddition. We therefore investigated this approach and report here the successful use of this chemistry for the formation of compound **2** (R = H) and hence a formal synthesis of deethylibophyllidine.[17]



Scheme 1. Retrosynthesis.

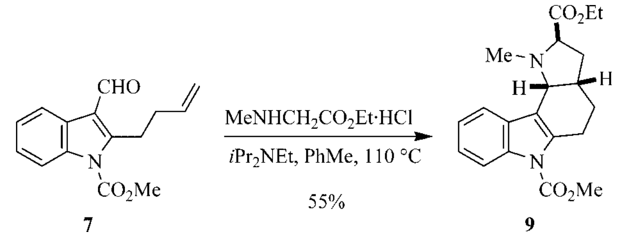
Results and Discussion

We needed a synthetic route to the aldehyde **7** in preparation for the key cycloaddition reactions. A route to the indole **5**, containing the required 2-butenyl chain, has been described in the literature,[18] however this was lengthy and low-yielding. We therefore explored the possibility of a shorter route by carrying out a *C*-allylation of the dianion generated from commercially available 2-methylindole (**4**). The dianion of **4** can be prepared by double deprotonation in the presence of a strong base and has been reported to undergo methylation to give 2-ethylindole.[19] Using these conditions, but with allyl bromide rather than iodomethane as the electrophile, the product **5** was formed in reasonable yield (Scheme 2). The deprotonation was best conducted using either freshly sublimed *t*BuOK, or more easily, a solution of *t*BuOK in THF. The absence of either *t*BuOK or *n*BuLi resulted in only recovered starting material **4**. Formylation of the indole **5** was conducted under standard conditions with $POCl_3$ and DMF, and the product **6** was converted into the aldehyde **7** by treatment with methyl chloroformate and the base sodium hexamethyldisilazide (NaHMDS) (or in similar yield under phase-transfer conditions with 30% NaOH and 0.05 equiv. $BnEt_3NCl$ in CH_2Cl_2 at 0 °C). Alternatively, the aldehyde **6** was protected as the *N*-Boc derivative **8** by treatment with Boc_2O.



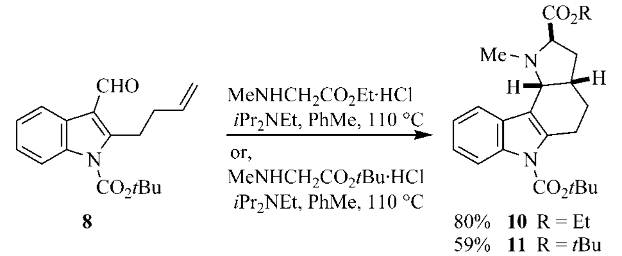
Scheme 2. Preparation of the aldehydes **7** and **8**.

Initial attempts to form the azomethine ylide and hence to investigate the potential for intramolecular cycloaddition were performed using *N*-methylglycine ethyl ester (sarcosine ethyl ester). Using an excess of this secondary amine as its hydrochloride salt with the aldehyde **7** and diisopropylethylamine and heating under reflux in toluene gave the desired cycloadduct **9** (Scheme 3). The structure of the product was verified by ^1H NMR spectroscopic analysis, and this showed one major stereoisomer with a small amount of what was probably another, inseparable, diastereomer. The relative stereochemistry of this racemic major isomer was confirmed by NOE spectroscopy. This showed the *cis* ring-fused arrangement with the ethyl ester substituent *cis* to these ring junction protons. This relative stereochemistry conforms to cycloaddition through the expected S-shaped azomethine ylide.[13] Attempted cycloaddition using the aldehyde **6** was unsuccessful.



Scheme 3. Cycloaddition with sarcosine ethyl ester.

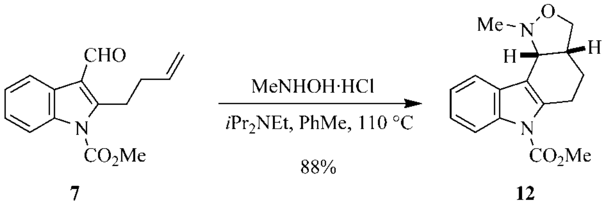
Further examples of this type of cycloaddition of ester-stabilised azomethine ylides are provided in Scheme 4, using the aldehyde **8**. The products **10** and **11** were formed in good yield and as predominantly one stereoisomer (*dr* ≈ 7:1 based on ^1H NMR spectroscopic analysis). As before, NOE spectroscopy was used to verify the relative stereochemistry and the coupling constant between the ring junction protons was the same as that for the cycloadduct **9** (*J* 6.0 Hz), indicating a *cis* fused arrangement.



Scheme 4. Further ester-stabilised ylide cycloadditions.

To show that this chemistry is amenable to other dipoles, treatment of the aldehyde **7** with *N*-methylhydroxylamine gave the intermediate nitrone and hence the cycloadduct **12** (Scheme 5). This was formed as a single stereoisomer in good yield. To confirm the *cis* stereochemistry at the ring junction, the cycloadduct **12** was converted to compound

13 by reduction of the N–O bond with zinc/AcOH and treatment with *p*-bromobenzoyl chloride; subsequent X-ray crystallographic structure analysis of the diacylated compound **13** verified the expected structure and stereochemistry (Figure 2).



Scheme 5. Nitrone cycloaddition.

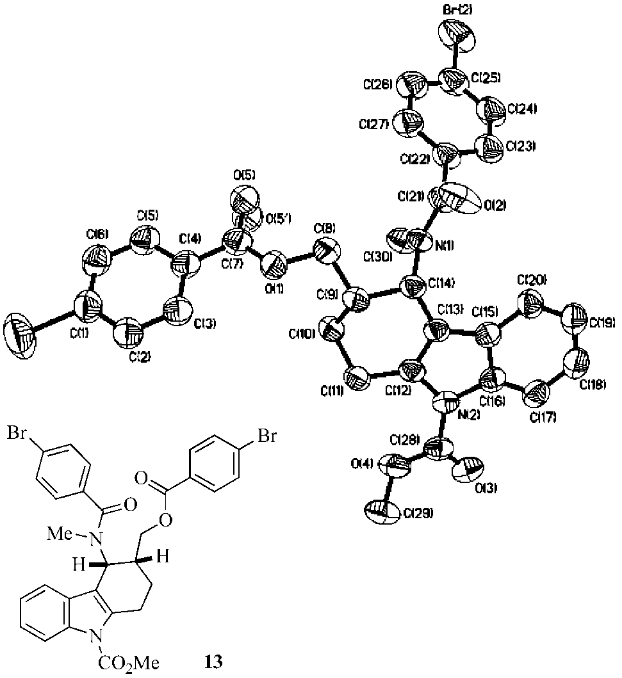
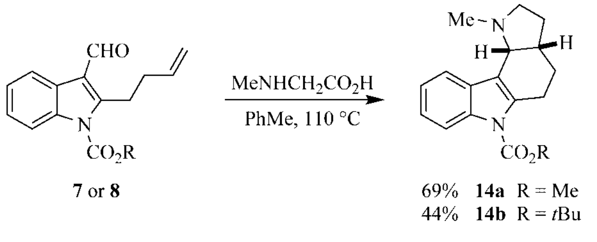


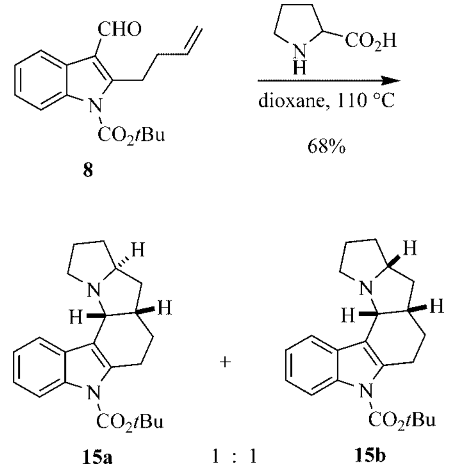
Figure 2. Structure and ORTEP plot of ester **13**.

We then investigated the cycloaddition with non-stabilised azomethine ylides generated from the aldehydes **7** and **8** and amino acids. In particular, heating these aldehydes with *N*-methylglycine in toluene gave the desired cycloadducts **14a** and **14b** (Scheme 6). In both cases only the *cis* ring-fused product was observed, and this was confirmed for the product **14b** by NOE spectroscopy.



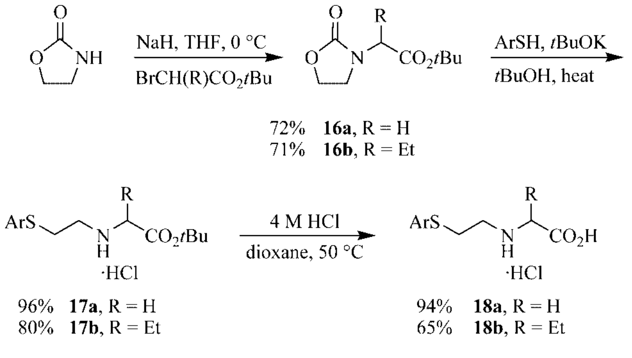
Scheme 6. Cycloaddition with sarcosine.

Cycloaddition of the aldehyde **8** was also studied using the amino acid proline (Scheme 7). A mixture of two stereoisomeric products was obtained. These were separable by column chromatography on silica. The products correspond to the stereoisomers **15**, in which the ring junction protons are *cis* to one another (confirmed by the coupling constants and by NOE spectroscopy on one of the isomers).



Scheme 7. Cycloaddition with proline.

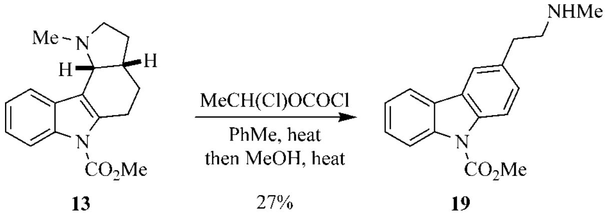
Application of this chemistry to the ibophyllidine alkaloid ring system would ideally make use of an appropriate *N*-substituted amino acid to condense with the aldehyde **7**. In particular, we envisaged that an *N*-arylthioethyl substituent would provide direct access to the required carbon skeleton for these alkaloids that would be suitable for subsequent *S*-oxidation (to give compound **1**) and Pummerer cyclisation. The amino acids **18**, R = H or Et were prepared from 2-oxazolidinone (Scheme 8). Initial *N*-alkylation using NaH as the base proceeded efficiently with either *tert*-butyl bromoacetate or *tert*-butyl bromobutyrate to give the oxazolidinones **16a** and **16b**. These were opened with *para*-chlorothiophenol and *t*BuOK as the base, following conditions for related reactions reported by Ishibashi and co-workers.[20] Finally, ester hydrolysis with HCl in dioxane gave the desired amino acids **18** as their hydrochloride salts. This represents an efficient entry to *N*-arylthioethyl amino acids.



Scheme 8. Preparation of *N*-arylthioethyl amino acids (Ar = *p*-ClC$_6$H$_4$).

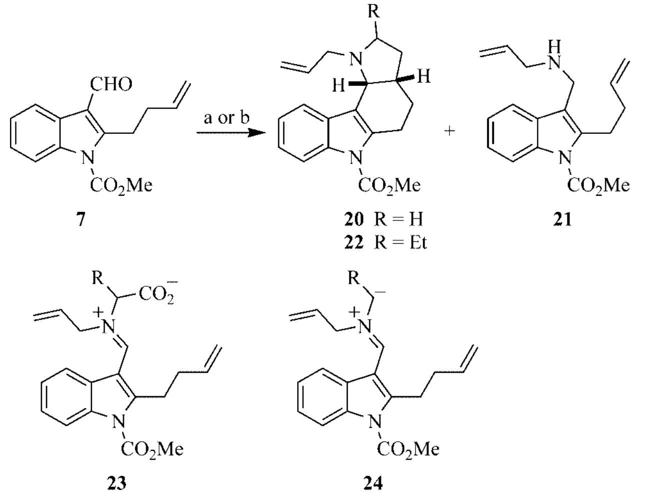
We were disappointed to find that all attempts to effect cycloadditions of the aldehydes **7** or **8** with the amino acids **18a** or **18b** (or with the amino esters **17**) failed. In all cases only recovered aldehyde was obtained together with, under more forcing conditions, some of the aldehyde **6**, in which the *N*-protecting group had been removed. Treatment of the amino acid **18a** with two equivalents of aqueous NaOH (in H_2O/THF, 1:1) gave the corresponding sodium carboxylate (after removal of the solvent by evaporation); however, attempts to use this sodium salt in the cycloaddition also resulted in no reaction and only the starting aldehyde **7** was recovered. It is possible that the sulfur atom participates to trap the intermediate iminium ion; hydrolysis of the resulting *S*-arylthiazolidinium ion would re-form the aldehyde **7**.

With the failure of the amino acids **18** to undergo cycloaddition with the aldehyde **7**, we needed an alternative strategy. We could have selected a different *N*-alkyl group, but we chose first to explore the demethylation of the cycloadduct **14a**. One approach to demethylation of amines involves the use of α-chloroethyl chloroformate followed by heating the intermediate carbamate with methanol.[21] Treating the amine **14a** under these conditions gave, not the desired demethylated compound, but the carbazole **19** in low yield (Scheme 9). This product likely arises from the desired *N*-acylation, but instead of displacement of the methyl group by the chloride ion, the molecule fragments with breakage of the benzylic C–N bond. Subsequent elimination and aromatisation (plus hydrolysis of the chloroethyl carbamate) provides **19**.



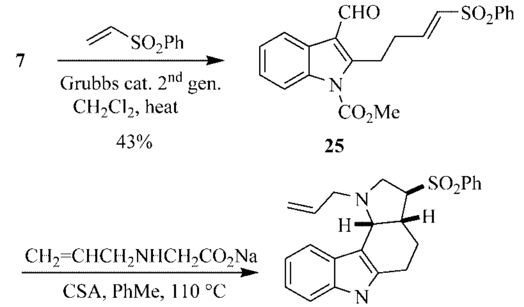
Scheme 9. Attempted demethylation of **14a**.

We therefore turned to the use of an *N*-alkyl group that should be more readily removed from the cycloadduct. For this we chose the *N*-allyl group and prepared *N*-allylglycine by hydrolysis with NaOH of *N*-allylglycine ethyl ester.[22] In the same way, we also prepared 2-(allylamino)butyric acid by hydrolysis of ethyl 2-(allylamino)butyrate, itself prepared by addition of allylamine to ethyl 2-bromobutyrate. Heating the aldehyde **7** with *N*-allylglycine in toluene with camphorsulfonic acid gave the desired cycloadduct **20** in moderate yield (Scheme 10). Only one stereoisomer was formed, which was assumed to have *cis* ring junction protons by analogy with previous examples (coupling constant, J = 5.5 Hz in the ^{1}H NMR spectrum). A by-product in this reaction was also formed and was difficult to separate from the cycloadduct **20**. However, by careful column chromatography some of the amine **21** was isolated. To obtain a pure sample of the cycloadduct **20** it was found preferable to treat the mixture of **20** and **21** with methyl chloroformate, as this reacts with the amine **21**, and then to perform column chromatography. Heating the aldehyde **7** with 2-(allylamino)butyric acid gave some cycloadduct **22**. This product was isolated in low yield as a single stereoisomer (stereochemistry undetermined). In this case the by-product **21** was formed as the major product. We presume that the secondary amine **21** arises either from the intermediate iminium ion **23** that undergoes isomerisation into conjugation with the carboxylate, followed by hydrolysis, or by protonation of the azomethine ylide **24** followed by hydrolysis of the iminium ion.



Scheme 10. Cycloaddition with *N*-allylglycine and 2-(allylamino)butyric acid. a) CH_2=$CHCH_2NHCH_2CO_2Na$, PhMe, CSA, heat gave **20**, 42% and **21**, <10%; b) CH_2=$CHCH_2NHCH(Et)CO_2Na$, PhMe, TsOH, heat gave **22**, 19% and **21**, 60%.

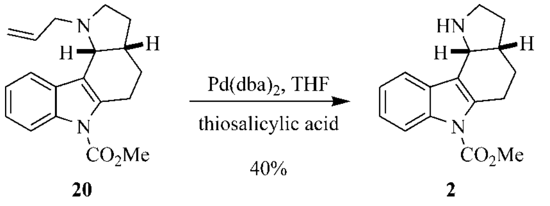
Although intramolecular dipolar cycloaddition reactions are normally effective with unactivated alkenes as dipolarophiles, we considered activating the alkene in the substrate **7**. This was achieved by conversion to the sulfone **25** using cross-metathesis (Scheme 11). Treatment of the sulfone **25** with *N*-allylglycine gave the desired cycloadduct **26**. The yield of this product was improved in comparison to the cycloaddition in the absence of the sulfone substituent. None of the by-product akin to compound **21** was observed. A single stereoisomer of the cycloadduct **26** was produced, of undetermined stereochemistry, although based on the examples described above this is likely to be the isomer shown in Scheme 11. The chemistry therefore verifies the expected improvement of the efficiency of the cycloaddition in the presence of a sulfone substituent as an



Scheme 11. Cycloaddition with activated dipolarophile.

activating group, and this strategy could find use in other examples.[14d] With some of compound **20** to hand, however, we did not explore further the use of the activated substrate **25**.

All that was required to complete the formal synthesis of racemic deethylibophyllidine was the *N*-deallylation of compound **20** to give compound **2**, R = H. In the presence of $Pd(dba)_2$, dppb and thiosalicylic acid,[23] the allyl group was removed to give the desired product **2**, R = H (Scheme 12). The spectroscopic data for this compound matched that reported in the literature.[7] The preparation of this compound therefore completes a formal total synthesis of the natural product deethylibophyllidine. Overall, the tetracycle **2**, R = H is formed from 2-methylindole in only 5 steps.



Scheme 12. Deallylation and completion of formal synthesis.

Conclusions

A short synthesis of a variety of tetracyclic amines containing an indole unit has been accomplished. The chemistry uses an intramolecular [3+2] cycloaddition reaction of an azomethine ylide as its key step. The cycloaddition reaction sets up two new rings in a single step and is highly stereoselective, with formation of only the *cis*-fused 6,5-ring junction. The methodology has been applied to a formal synthesis of the natural product deethylibophyllidine.

Experimental Section

General Comments: All experiments were carried out under argon or nitrogen with freshly distilled solvents. Diethyl ether (Et_2O) and THF were distilled from sodium/benzophenone or were purified using a Grubbs solvent purification system.[24] Petrol refers to light petroleum (b.p. 40–60 °C). Column chromatography was performed on silica gel (230–400 mesh). Infrared spectra were recorded with a Nicolet Magna 550 FT-IR spectrometer or with a Perkin–Elmer Spectrum RX1/FT IR system with a DuraSampl IR-II diamond ATR. ^1H and ^{13}C NMR spectra were run with Bruker instruments at various field strengths as indicated. Chemical shifts are reported in parts per million (ppm) relative to solvent signals and coupling constants, *J*, are given in Hz (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Mass spectra were run with a Micromass GCT instrument or Micromass LCT. Low-resolution mass spectra were recorded with a Thermoquest CE Trace GCMS2000 series instrument fitted with a Restek RTX-5MS (Cross bond 5% diphenyl, 95% dimethyl polysiloxane 15-m column) with helium as the carrier gas using either EI or CI mode. Microanalysis was performed with a Carlo–Erba 1110 instrument.

2-(But-3-enyl)-1*H*-indole (5): *n*BuLi (60 mL, 150 mmol, 2.5 M in hexanes) was added to 2-methylindole (6.56 g, 50 mmol) and Et_2O (150 mL), followed by *t*BuOK (100 mL, 100 mmol, 1.0 M in THF), keeping the temperature below 20 °C. After 30 min the yellow solution was cooled to –78 °C. Allyl bromide (8.65 mL, 10 mmol) was added dropwise over 45 min. After 2 h at –78 °C, MeOH (30 mL) was added and the mixture was warmed to room temperature and stirred for a further 1 h. MeOH (150 mL) and silica were added and the solution was evaporated. Purification by column chromatography, eluting with petrol/EtOAc (95:5), gave the indole **5** (5.84 g, 68%) as an oil; $R_f = 0.61$ [petrol/EtOAc (4:1)]. IR (neat): $\tilde{\nu}_{max}$ = 3405, 3075, 2920, 1640, 1615, 1585 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 7.71 (br. s, 1 H, NH), 7.56–7.49 (m, 1 H, ArH), 7.25–7.19 (m, 3 H, ArH), 6.24 (s, 1 H, CH), 5.89 (ddt, *J* = 17, 10, 6.5 Hz, 1 H, CH=), 5.16–4.97 (m, 2 H, $=CH_2$), 2.77 (t, *J* = 7.5 Hz, 2 H, CH_2) 2.49–2.32 (m, 2 H, CH_2) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 139.3 (C), 137.8 (CH), 136.0 (C), 128.8 (C), 121.1 (CH), 119.9 (CH), 119.7 (CH), 115.7 (CH_2), 110.5 (CH), 99.7 (CH), 33.3 (CH_2), 27.7 (CH_2) ppm. HRMS (ES) found: [M^+], 171.1054, $C_{12}H_{13}N$ requires [M^+], 171.1048; data matches that in the literature.[18]

2-(But-3-enyl)-1*H*-indole-3-carbaldehyde (6): $POCl_3$ (10.7 mL, 116 mmol) was added to DMF (9.5 mL, 116 mmol) in CH_2Cl_2 (30 mL) at 0 °C over 30 min. The indole **5** (6.59 g, 39 mmol) in CH_2Cl_2 (30 mL) was added, keeping the temperature below 10 °C. The mixture was heated under reflux for 1 h, NaOH (20 mL, 2 M) was added and further heated under reflux for 1 h. The mixture was cooled to room temperature, neutralised using NaOH (100 mL, 2 M) and extracted with CH_2Cl_2 (4 × 75 mL). The organic phases were dried ($MgSO_4$), filtered and the solvents evaporated. Purification by column chromatography, eluting with petrol/EtOAc (7:3), followed by recrystallisation from petrol/EtOAc (1:1) gave the aldehyde **6** (6.35 g, 83%) as plates; m.p. 140–141 °C (dec.). $R_f = 0.34$ [petrol/EtOAc (1:1)]. IR (neat): $\tilde{\nu}_{max}$ = 3080, 2795, 1615, 1580 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 10.27 (s, 1 H, CHO), 9.72 (s, 1 H, NH), 8.41–8.32 (m, 1 H, ArH), 7.50–7.43 (m, 1 H, ArH), 7.40–7.30 (m, 2 H, ArH), 5.96 (ddt, *J* = 17.0, 10.5, 6.5 Hz, 1 H, $C\mathit{H}{=}CH_2$), 5.25–5.12 (2 H, m $CH{=}C\mathit{H_2}$), 3.30 (t, *J* = 7.5 Hz, 1 H, CH_2), 2.65 (dt, *J* = 7.5, 6.5 Hz, 2 H, CH_2) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 184.7 (C=O), 136.4 (CH), 136.3 (C), 126.0 (C), 123.6 (CH), 122.9 (CH), 121.0 (CH), 121.1 (C), 116.9 (CH_2), 114.3 (C), 111.2 (CH), 33.9 (CH_2), 25.9 (CH_2) ppm. HRMS (ES) found: [MH^+], 200.1073, $C_{13}H_{14}NO$ requires [MH^+], 200.1075; LRMS (ES): *m*/*z* = 200 (100) [MH^+], 172 (8) [MH^+ – CO]. $C_{13}H_{13}NO$ (199.10): calcd. C 78.36, H 6.58, N 7.03; found C 77.98, H 6.51, N 6.93.

Methyl 2-(But-3-enyl)-3-formyl-1*H*-indole-1-carboxylate (7): NaHMDS (18.6 mL, 18.6 mmol of a 1.0 M solution in THF) was added to the indole **6** (3.08 g, 15.5 mmol) in THF (200 mL) at –78 °C. After 30 min MeOCOCl (1.56 mL, 20.1 mmol) was added dropwise. After 90 min MeOH (25 mL) was added, and the mixture was warmed to room temperature. The solvent was evaporated and the residue was purified by column chromatography, eluting with petrol/EtOAc (7:3), followed by recrystallisation from petrol/EtOAc (1:1), to give the indole **7** (3.0 g, 78%) as needles; m.p. 81–82 °C. $R_f = 0.29$ [petrol/EtOAc (4:1)]. IR (neat): $\tilde{\nu}_{max}$ = 3065, 2955, 1740, 1655, 1605, 1555 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 10.28 (s, 1 H, CHO), 8.35–8.27 (m, 1 H, ArH), 8.06–7.98 (m, 1 H, ArH), 7.38–7.30 (m, 2 H, ArH), 5.86 (ddt, *J* = 17.0, 10.5, 7.0 Hz, 1 H, $C\mathit{H}{=}CH_2$), 5.12–5.06 (m, 2 H, $CH{=}C\mathit{H_2}$), 4.12 (s, 3 H, OCH_3), 3.49 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.48 (q, *J* = 7.5 Hz, 2 H, CH_2) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 186.0 (C=O), 151.8 (C=O), 136.4 (CH), 135.4 (C), 126.0 (C), 125.4 (CH), 124.6 (CH), 121.2 (CH), 118.8 (C), 116.4 (C and CH_2), 115.3 (CH), 54.3 (CH_3), 34.3 (CH_2), 25.8 (CH_2) ppm. HRMS (ES) found: [MH^+], 258.1130, $C_{15}H_{16}NO_3$

requires [MH$^+$], 258.1143; LRMS (ES): *m/z* = 258 (100) [MH$^+$]. $C_{15}H_{15}NO_3$ (257.11): calcd. C 70.02, H 5.88, N 5.44; found C 69.76, H 6.06, N 5.38.

***tert*-Butyl 2-(But-3-enyl)-3-formyl-1*H*-indole-1-carboxylate (8):** Et_3N (1.5 mL, 10.5 mmol), 4-(dimethylamino)pyridine (128 mg, 1.05 mmol) and Boc_2O (2.29 g, 10.5 mmol) was added to a stirred solution of the indole **6** (2.09 g, 10.5 mmol) in CH_2Cl_2 (50 mL) at 0 °C. After 16 h the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol/EtOAc (4:1), to give the indole **8** (2.91 g, 90%) as needles; m.p. 67–68 °C. R_f = 0.90 [petrol/EtOAc (4:1)]. IR (neat): $\tilde{\nu}_{max}$ = 3085, 2980, 1735, 1660, 1550 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 10.28 (s, 1 H, CHO), 8.34–8.28 (m, 1 H, ArH), 8.09–8.01 (m, 1 H, ArH), 7.37–7.29 (m, 2 H, ArH), 5.86 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1 H, C*H*=CH_2), 5.12–5.00 (2 H, m CH=C*H*$_2$), 3.50 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.49 (q, *J* = 7.5 Hz, 2 H, CH_2), 1.71 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 185.9 (C=O), 151.7 (C=O), 149.5 (C), 136.4 (CH), 135.8 (C), 126.0 (C), 125.0 (CH), 124.4 (CH), 121.1 (CH), 118.3 (C), 116.3 (CH_2), 115.2 (CH), 85.7 (C), 34.5 (CH_2), 28.1 (CH_3), 25.7 (CH_2) ppm. HRMS (ES) found: [MNa$^+$], 322.1419, $C_{18}H_{21}NO_3Na$ requires [MNa$^+$], 322.1420; LRMS (ES): *m/z* (%) 322 (6) [MNa$^+$], 244 (100). $C_{18}H_{21}NO_3$ (299.15): calcd. C 72.22, H 7.07, N 4.68; found C 72.14, H 7.16, N 4.50.

6-Methyl 1-Ethyl 1-Methyl-2,3,3a,4,5,10c-hexahydro-1*H*-pyrrolo-[3,2-*c*]carbazole-2,6-dicarboxylate (9): *N*-Methylglycine ethyl ester hydrochloride (337 mg, 2.2 mmol) and diisopropylethylamine (0.48 mL, 2.8 mmol) was added to a stirred solution of the aldehyde **7** (141 mg, 0.55 mmol) in toluene (5 mL), and the mixture was heated under reflux. After 16 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol/EtOAc (7:3), to give the amine **9** (107 mg, 55%) as an oil. R_f = 0.34 [petrol/EtOAc (7:3)]. IR (neat): $\tilde{\nu}_{max}$ = 2945, 1735, 1605 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.05–7.97 (m, 1 H, ArH), 7.57–7.50 (m, 1 H, ArH), 7.18–7.10 (m, 2 H, ArH), 4.32–4.27 (d, *J* = 6.0 Hz, 1 H, NCH), 4.14 (q, *J* = 7.0 Hz, 2 H, OCH_2), 3.92 (s, 3 H, OCH_3), 3.75 (dd, *J* = 8.5, 4.5 Hz, 1 H, CHCO), 3.12 (dt, *J* = 18.5, 5.0 Hz, 1 H, CH), 2.92–2.73 (m, 1 H, CH), 2.46 (s, 3 H, NCH_3), 2.42–2.27 (m, 1 H, CH), 2.25–2.10 (m, 1 H, CH), 1.99–1.82 (m, 2 H, 2 × CH), 1.81–1.66 (m, 1 H, CH), 1.24 (t, *J* = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 174.3 (C=O), 153.0 (C=O), 138.4 (C), 135.9 (C), 130.2 (C), 123.6 (CH), 122.9 (CH), 118.6 (CH), 116.0 (C), 115.5 (CH), 64.7 (CH_3), 60.3 (CH_2), 57.3 (CH_3), 53.4 (CH), 37.0 (CH), 36.2 (CH), 34.0 (CH_2), 27.8 (CH_2), 24.7 (CH_2), 14.5 (CH_3) ppm. HRMS (ES) found: [MH$^+$], 357.1812, $C_{20}H_{25}N_2O_4$ requires [MH$^+$], 357.1814; LRMS (ES): *m/z* (%) = 357 (100) [MH$^+$], 326 (9).

6-*tert*-Butyl 2-Ethyl 1-Methyl-2,3,3a,4,5,10c-hexahydro-1*H*-pyrrolo-[3,2-*c*]carbazole-2,6-dicarboxylate (10): *N*-Methylglycine ethyl ester hydrochloride (630 mg, 4.1 mmol) and diisopropylethylamine (0.88 mL, 5.1 mmol) was added to a stirred solution of the aldehyde **8** (305 mg, 1.0 mmol) in toluene (5 mL), and the mixture was heated under reflux. After 18 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol/EtOAc (9:1), to give the amine **10** (324 mg, 80%) as an oil. R_f = 0.33 [petrol/EtOAc (4:1)]. IR (neat): $\tilde{\nu}_{max}$ = 2980, 1725, 1665 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15–8.11 (m, 1 H, ArH), 7.62–7.60 (m, 1 H, ArH), 7.26–7.18 (m, 2 H, ArH), 4.39 (d, *J* = 6.0 Hz, 1 H, NCH), 4.23 (q, *J* = 7.0 Hz, 2 H, OCH_2), 3.82 (dd, *J* = 8.5, 4.5 Hz, 1 H, CH), 3.20 (dt, *J* = 18.0, 5.0 Hz, 1 H, CH), 2.95 (ddd, *J* = 18.0, 9.5, 6.0 Hz, 1 H, CH), 2.55 (s, 3 H, NCH_3), 2.49–2.41 (m, 1 H, CH), 2.24 (ddd, *J* = 13.0, 8.0, 5.0 Hz, 1 H, CH), 2.02 (ddd, *J* = 13.0, 9.0, 3.5 Hz, 1 H, CH), 1.99–1.92 (m, 1 H, CH), 1.86–1.78 (m, 1 H, CH), 1.66 (s, 9 H, *t*Bu), 1.33 (t, *J* = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.3 (C=O), 150.5 (C=O), 138.2 (C), 136.0 (C), 130.0 (C), 123.2 (CH), 122.4 (CH), 118.4 (CH), 115.5 (CH), 115.3 (C), 83.5 (C), 64.6 (CH), 60.1 (CH_2), 57.1 (CH), 36.9 (CH_3), 36.1 (CH), 33.9 (CH_2), 28.2 (CH_3), 27.8 (CH_2), 24.8 (CH_2), 14.4 (CH_3) ppm. HRMS (ES) found: [MH$^+$], 399.2281, $C_{23}H_{31}N_2O_4$ requires [MH$^+$], 399.2284. LRMS (ES): *m/z* (%) = 399 (100) [MH$^+$], 343 (40).

2,6-Di-*tert*-Butyl 1-Methyl-2,3,3a,4,5,10c-hexahydro-1*H*-pyrrolo-[3,2-*c*]carbazole-2,6-dicarboxylate (11): *N*-Methylglycine *tert*-butyl ester hydrochloride (874 mg, 4.8 mmol) and diisopropylethylamine (1.66 mL, 9.5 mmol) was added to a stirred solution of the aldehyde **8** (569 mg, 1.2 mmol) in toluene (5 mL), and the mixture was heated under reflux. After 96 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol/EtOAc (4:1), to give the amine **11** (299 mg, 59%) as an oil. R_f = 0.42 [petrol/EtOAc (4:1)]. IR (neat): ṽmax = 3065, 2930, 1730, 1640, 1605, 1575 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21–8.15 (m, 1 H, ArH), 7.69–7.64 (m, 1 H, ArH), 7.30–7.20 (m, 2 H, ArH), 4.42 (d, *J* = 6.0 Hz, 1 H, NCH), 3.78 (dd, *J* = 8.5, 4.5 Hz, 1 H, CH), 3.23 (dt, *J* = 18.0, 5.0 Hz, 1 H, CH), 2.88–2.79 (m, 1 H, CH), 2.63 (s, 3 H, NCH_3), 2.51–2.42 (m, 1 H, CH), 2.24 (ddd, *J* = 13.0, 8.0, 4.5 Hz, 1 H, CH), 2.08–1.95 (m, 2 H, 2 CH), 1.90–1.81 (m, 1 H, CH), 1.69 (s, 9 H, *t*Bu), 1.57 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.0 (C=O), 150.6 (C=O), 138.3 (C), 136.0 (C), 130.1 (C), 123.3 (CH), 122.7 (CH), 118.5 (CH), 115.8 (C), 115.5 (CH), 83.5 (C), 80.8 (C), 65.4 (CH), 57.1 (CH), 36.9 (CH_3), 36.2 (CH), 34.1 (CH_2), 28.31 (CH_3), 28.28 (CH_3), 28.2 (CH_2), 24.9 (CH2) ppm. HRMS (ES) found: [MH$^+$], 427.2603, $C_{25}H_{35}N_2O_4$ requires [MH$^+$], 427.2597; LRMS (ES): *m/z* (%) = 427 (88) [MH$^+$], 371 (100), 315 (49).

Methyl 1-Methyl-1,3,3a,4,5,10c-hexahydro-2-oxa-1,6-diazacyclopenta[*c*]fluorene-6-carboxylate (12): A solution of the aldehyde **7** (132 mg, 0.52 mmol), *N*-methylhydroxylamine hydrochloride (64 mg, 0.77 mmol) and diisopropylethylamine (0.13 mL, 0.77 mmol) in toluene (10 mL) was heated under reflux. After 90 min, the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol/EtOAc (3:2), to give the indole **12** (130 mg, 88%) as an oil. R_f = 0.50 [petrol/EtOAc (3:2)]. IR (neat): $\tilde{\nu}_{max}$ = 2945, 2865, 1735, 1610, 1580 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.04–8.00 (m, 1 H, ArH), 7.51–7.43 (m, 1 H, ArH), 7.22–7.13 (m, 2 H, ArH), 4.22 (t, *J* = 8.0 Hz, 1 H, OCH), 3.94 (s, 3 H, OCH_3), 3.86–3.81 (br, 1 H, NCH), 3.74–3.65 (m, 1 H, OCH), 3.16–3.06 (br. m, 1 H, CH), 2.99–2.86 (m, 2 H, 2 CH), 2.84 (s, 3 H, NCH_3), 2.19–2.12 (m, 1 H, CH), 1.95–1.86 (m, 1 H, CH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.4 (C=O), 138.0 (C), 136.0 (C), 129.1 (C), 123.8 (CH), 123.0 (CH), 117.8 (CH), 115.5 (CH), 113.8 (C), 70.0 (CH_2), 63.5 (CH), 53.4 (CH_3), 44.9 (CH_3), 40.0 (CH), 24.8 (CH_2), 22.8 (CH_2) ppm. HRMS (ES) found: [MH$^+$], 287.1397, $C_{16}H_{19}N_2O_3$ requires [MH$^+$], 287.1396; LRMS (ES): *m/z* (%) = 287 (100) [MH$^+$].

Methyl 4-[(4-Bromobenzoyl)methylamino]-3-(4-bromobenzoyloxymethyl)-1,2,3,4-tetrahydrocarbazole-9-carboxylate (13): A solution of the cycloadduct **12** (126 mg, 0.44 mmol), acetic acid (1.7 mL), water (3.3 mL) and zinc (121 mg, 1.8 mmol) was heated at 70 °C. After 2 h, the mixture was filtered through Celite, the solvent was evaporated and the residue was extracted from 10% aqueous NH_4OH with CH_2Cl_2 (4 × 20 mL), dried ($MgSO_4$) and the solvents evaporated. To the residue was added CH_2Cl_2 (10 mL), 4-dimethylaminopyridine (54 mg, 0.44 mmol), Et_3N (0.37 mL, 2.6 mmol) and 4-bromobenzoyl chloride (480 mg, 2.2 mmol) at room temperature. After 16 h, aqueous $NaHCO_3$ (25 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 20 mL), dried ($MgSO_4$) and the solvents evaporated. The solid product was recrystallised from petrol/EtOAc to give the ester **13** (183 mg, 63%) as cubes; m.p. 190–191 °C. R_f = 0.42 [petrol/EtOAc (7:3)]. IR (neat): $\tilde{\nu}_{max}$ = 3340, 3060, 2970, 2920, 2855, 1735, 1715, 1630, 1590 cm^{-1}. ^1H NMR(250 MHz, $CDCl_3$) 8.06 (d, 1 H, *J* 8.5, ArH), 7.94–7.85 (m, 3 H, ArH), 7.64–7.42 (m, 4 H, ArH), 7.32–7.17 (m, 4 H, ArH), 6.47 (d, 1 H, *J* 5.5, CH), 4.59–4.44 (m, 2 H, CH_2), 4.00 (s, 3 H, OCH_3), 3.40 (dd, 1 H, *J* 18.0, 5.0, CH), 3.00–2.91 (m, 1 H, CH), 2.62 (s, 3 H, NCH_3), 2.60–2.55 (m, 1 H, CH), 2.12–2.04 (m, 1 H, CH), 1.88–1.77 (m, 1 H, CH). ^{13}C NMR (100 MHz, $CDCl_3$) 171.6 (C=O), 166.0 (C=O), 152.3 (C=O), 138.9 (C), 135.9 (C), 135.6 (C), 131.7 (CH), 131.3 (CH), 130.2 (C), 128.9 (C), 128.2 (CH), 128.2 (C), 124.5 (CH), 123.7 (C), 123.6 (CH), 118.3 (CH), 115.6 (CH), 114.5 (C), 65.6 (CH_2), 53.6 (CH_3), 45.2 (CH), 37.8 (CH_3), 35.5 (CH), 24.6 (CH_2), 23.1 (CH_2). HRMS (ES) found: [MNa^+], 675.0081, $C_{30}H_{26}Br_2N_2O_5Na$ requires [MNa^+], 675.0106. LRMS (ES): *m*/*z* (%) = 677 (14) [MNa^+], 655 (7) [MH], 442 (97), 440 (100). $C_{30}H_{26}Br_2N_2O_5$ (652.02): calcd. C 55.07, H 4.00, Br 24.42, N 4.28; found C 55.29, H 3.88, Br 24.31, N 4.09.

X-ray Crystallography of Ester 13: Triclinic crystal system, space group $P\bar{1}$. Unit cell dimensions a = 9.3822(4) Å, α = 85.372(2)°, b = 11.6384(5) Å, β = 76.381(2)°, c = 13.3734(6) Å, γ = 83.273(2)°, V = 1407.33(11) $Å^3$, Z = 2, $d_{calcd.}$ = 1.544 mg/m^3. Absorption coefficient = 2.922 mm^{-1}. F(000) = 660. Crystal size 0.35 × 0.28 × 0.19 mm^3. Reflections collected 34124, independent reflections 6043 [R_{int} = 0.0347]. Full-matrix least-squares on F^2 refinement method. Goodness-of-fit on F^2 = 1.074.

CCDC-629950 contains supplementary crystallographic data for **13**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

6-Methyl 1-Methyl-2,3,3a,4,5,10c-hexahydro-1*H*-pyrrolo[3,2-*c*]carbazole-6-carboxylate (14a): *N*-methylglycine (178 mg, 1.9 mmol) was added to a stirred solution of the aldehyde **7** (128 mg, 0.5 mmol) in toluene (10 mL) and the mixture was heated under reflux. After 21 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with CH_2Cl_2/MeOH (95:5), to give the amine **14a** (141 mg, 69%) as an oil. R_f = 0.22 [CH_2Cl_2/MeOH (9:1)]. IR (neat): $\tilde{\nu}_{max}$ = 2950, 1725, 1610 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.21–8.06 (m, 1 H, ArH), 7.54–7.51 (m, 1 H, ArH), 7.20–7.12 (m, 2 H, ArH), 3.93 (s, 3 H, OCH_3), 3.49 (d, *J* = 4.5 Hz, 1 H NCH), 3.29–3.24 (m, 1 H, CH), 3.23–3.19 (m, 1 H, CH), 2.87 (ddd, *J* = 17.5, 11.5, 6.0 Hz, 1 H, CH), 2.58 (s, 3 H, NCH_3), 2.51–2.45 (m, 1 H, CH), 2.34–2.22 (m, 1 H, CH), 2.20–2.12 (m, 1 H, CH), 2.13–2.01 (m, 1 H, CH), 1.92–1.87 (m, 1 H, CH), 1.59–1.51 (m, 1 H, CH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.4 (C=O), 138.5 (C), 136.0 (C), 130.0 (C), 123.5 (CH), 122.8 (CH), 118.5 (CH), 115.3 (CH), 115.1 (C), 61.4 (CH), 55.7 (CH_2), 53.4 (CH_3) 42.1 (CH_3), 36.7 (CH), 29.0 (CH_2), 27.7 (CH_2), 25.0 (CH_2) ppm. HRMS (ES) found: [MH^+], 285.1596, $C_{17}H_{21}N_2O_2$ requires [MH^+], 285.1603; LRMS (ES): *m*/*z* (%) = 285 (100) [MH^+].

6-*tert*-Butyl 1-Methyl-2,3,3a,4,5,10c-hexahydro-1*H*-pyrrolo[3,2-*c*]carbazole-6-carboxylate (14b): *N*-Methylglycine (554 mg, 6.2 mmol) was added to a stirred solution of the aldehyde **8** (400 mg, 1.55 mmol) in toluene (10 mL) and the mixture was heated under reflux. After 72 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with CH_2Cl_2/MeOH/NH_3 (99:1:0.1), to give the amine **14b** (194 mg, 44%) as an oil. R_f = 0.43 [CH_2Cl_2/MeOH (95:5)]. IR (neat): $\tilde{\nu}_{max}$ = 2935, 2765, 1725 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.5 Hz, 1 H, ArH), 7.47 (d, *J* = 8.5 Hz, 1 H, ArH), 7.16–7.07 (m, 2 H, ArH), 3.21 (d, *J* = 5.5 Hz, 1 H, CH), 3.18–3.10 (m, 1 H, CH), 3.10–3.05 (m, 1 H, CH), 2.79 (ddd, *J* = 17.5, 11, 6 Hz, 1 H, CH), 2.42 (s, 3 H, NCH_3), 2.32–2.25 (m, 1 H, CH), 2.17–2.09 (m, 1 H, CH), 2.05–1.93 (m, 2 H, 2 × CH), 1.78–1.70 (m, 1 H, CH), 1.56 (s, 9 H, *t*Bu), 1.53–1.47 (m, 1 H, CH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 150.5 (C=O), 138.1 (C), 136.1 (C), 129.9 (C), 123.5 (CH), 122.5 (CH), 118.3 (CH), 115.5 (C), 115.4 (CH), 83.4 (C), 61.3 (CH), 55.8 (CH_2), 42.3 (CH_3), 36.2 (CH), 29.0 (CH_2), 28.2 (CH_3), 28.1 (CH_2), 25.5 (CH_2) ppm. HRMS (ES) found: [MH^+], 327.2073, $C_{20}H_{27}N_2O_2$ requires [MH^+], 327.2060. LRMS (ES): *m*/*z* (%) = 327 (100) [MH^+], 271 (8).

Pentacycles 15a and 15b: Proline (348 mg, 3.0 mmol) was added to the aldehyde **8** (226 mg, 0.76 mmol) in dioxane (20 mL) and the mixture was heated at 110 °C. After 20 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with CH_2Cl_2/MeOH/NH_3 (95:5:0.1), to give the amines **15a** and **15b** (181 mg, 68%, 1:1) as oils; data for less polar product: R_f = 0.54 [CH_2Cl_2/MeOH/NH_3 (9:1:0.1)]. IR (neat): $\tilde{\nu}_{max}$ = 3050, 2925, 2865, 2800, 1725, 1605 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.12–8.07 (m, 1 H, ArH), 7.60–7.56 (m, 1 H, ArH), 7.23–7.16 (m, 2 H, ArH), 3.87 (d, *J* = 5.5 Hz, 1 H, CH), 3.86–3.80 (m, 1 H, CH), 3.40 (ddd, *J* = 9.5, 6.5, 3 Hz, 1 H, CH), 3.22 (ddd, *J* = 18, 6, 4 Hz, 1 H, CH), 3.04 (dt, *J* = 9.5, 6 Hz, 1 H, CH), 2.87 (ddd, *J* = 17, 10, 6 Hz, 1 H, CH), 2.57–2.50 (m, 1 H, CH), 2.11–1.99 (m, 3 H, 3 CH), 1.99–1.85 (m, 3 H, 3 CH), 1.78–1.69 (m, 1 H, CH), 1.64 (s, 9 H, *t*Bu), 1.52–1.43 (m, 1 H, CH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.6 (C=O), 136.3 (C), 136.1 (C), 129.5 (C), 123.2 (CH), 122.3 (CH), 118.4 (CH), 118.1 (C), 115.4 (CH), 83.3 (C), 64.4 (CH), 62.5 (CH), 56.8 (CH_2), 41.3 (CH), 40.2 (CH_2), 31.0 (CH_2), 28.2 (CH_3), 28.1 (CH_2), 25.6 (CH_2), 24.5 (CH_2) ppm. HRMS (ES) found: [M^+], 352.2161, $C_{22}H_{28}N_2O_2$ requires [M^+], 352.2151; LRMS (ES): *m*/*z* (%) = 352 (13) [M^+], 243 (100). NOESY on the less polar product was possible on selected isolated peaks and showed enhancement between the vicinal ring junction protons (α and β to the indole 3-position) (3.7 and 3.9%) and enhancement between the proton β to the indole 3-position and a vicinal proton (presumably *cis*) in the pyrrolidine (γ to the indole 3-position) (3.5 and 5.1%); in addition there was no enhancement between this proton at the γ position and the vicinal proton at the ring junction of the pyrrolidine (δ to the indole 3-position) that was added as proline – although not conclusive, this data suggests that the less polar product has the structure **15a**; data for more polar product: R_f = 0.44 [CH_2Cl_2/MeOH/NH_3 (9:1:0.1)]. IR (neat): $\tilde{\nu}_{max}$ = 3060, 2935, 2865, 1730, 1605 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.11–8.07 (m, 1 H, ArH), 7.84–7.98 (m, 1 H, ArH), 7.27–7.20 (m, 2 H, ArH), 4.46 (d, *J* = 5 Hz, 1 H, CH), 3.92–3.83 (m, 1 H, CH), 3.25 (ddd, *J* = 18, 5, 3 Hz, 1 H, CH), 2.87–2.79 (m, 1 H, CH), 2.78–2.72 (m, 1 H, CH), 2.72–2.65 (m, 1 H, CH), 2.49–2.42 (m, 1 H, CH), 2.42–2.34 (m, 1 H, CH), 2.22–2.14 (m, 1 H, CH), 2.05–1.97 (m, 1 H, CH), 1.87–1.78 (m, 2 H, 2 × CH), 1.67 (s, 9 H, *t*Bu), 1.65–1.56 (m, 1 H, CH), 1.47–1.39 (m, 2 H, 2 CH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.5 (C=O), 138.5 (C), 135.9 (C), 129.2 (C), 123.7 (CH), 122.9 (CH), 119.2 (CH), 117.1 (C), 115.2 (CH), 83.7 (C), 65.4 (CH), 57.9 (CH), 49.6 (CH_2), 39.6 (CH), 37.4 (CH_2), 32.7 (CH_2), 28.2 (CH_2), 28.1 (CH_3), 26.1 (CH_2), 25.3 (CH_2) ppm. HRMS (ES) found: [M^+], 352.2150, $C_{22}H_{28}N_2O_2$ requires [M^+], 352.2151; LRMS (ES): *m*/*z* (%) = 352 (9) [M^+], 243 (100).

***tert*-Butyl (2-Oxo-1,3-oxazolidin-3-yl)acetate (16a):** NaH (2.4 g, 60 mmol, 60% dispersion in mineral oil) was added to a stirred solution of 2-oxazolidinone (5.65 g, 58.6 mmol) in THF (80 mL) at 0 °C. After 30 min *tert*-butyl bromoacetate (13.0 mL, 87.9 mmol) was added dropwise. The mixture was warmed to room temperature over 16 h. Water (60 mL) was added followed by EtOAc

(60 mL), the phases were separated and the aqueous phase was extracted with EtOAc (4 × 50 mL). The combined organic phases were washed with brine (200 mL), dried ($MgSO_4$) and evaporated to give the oxazolidinone **16a** (11.8 g, 72%) as needles; m.p. 82–83 °C. R_f = 0.23 [petrol/EtOAc (1:1)]. IR (neat): $\tilde{\nu}_{max}$ = 2970, 1760, 1740 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ = 4.39–4.35 (t, *J* = 8.0 Hz, 2 H, CH_2), 3.92 (s, 2 H, CH_2), 3.73–3.68 (t, *J* = 8.0 Hz, 2 H, CH_2), 1.48 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 167.8 (C=O), 158.4 (C=O), 82.9 (C), 62.5 (CH_2), 46.5, (CH_2) 45.3 (CH_2), 28.4 (CH_3) ppm. HRMS (EI) found: [M^+], 201.1006, $C_9H_{15}NO_4$ requires [M^+], 201.1001; LRMS (EI): *m*/*z* (%) = 201 (2) [M^+], 101 (100). $C_9H_{15}NO_4$ (201.10): calcd. C 53.72, H 7.51, N 6.96; found C 53.79, H 7.25, N 6.97.

***tert*-Butyl (2-Oxo-1,3-oxazolidin-3-yl)butyrate (16b):** NaH (3.2 g, 135 mmol, 60% dispersion in mineral oil) was added to 2-oxazolidinone (10.65 g, 122 mmol) in THF (125 mL) at 0 °C. After 30 min *tert*-butyl 2-bromobutyrate (25.1 mL, 159 mmol) was added dropwise, then the mixture was heated under reflux for 16 h. Water (60 mL) was added followed by EtOAc (60 mL), the phases were separated and the aqueous phase was extracted with EtOAc (4 × 50 mL). The combined organic phases were washed with brine (200 mL), dried ($MgSO_4$) and the solvents evaporated. Purification by column chromatography, eluting with petrol/EtOAc (7:3), gave the oxazolidinone **16b** (19.8 g, 71%) as an oil. R_f = 0.53 [petrol/EtOAc (1:1)]. IR (neat): $\tilde{\nu}_{max}$ = 1740, 1735 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 4.34–4.23 (m, 2 H, CH_2), 4.17–4.13 (dd, *J* = 11.0, 5.0 Hz, 1 H, CH), 3.74–3.69 (m, 1 H, CH), 3.46–3.40 (m, 1 H, CH), 1.95–1.86 (m, 1 H, CH), 1.61–1.52 (m, 1 H, CH), 1.36 (s, 9 H, *t*Bu), 0.91–0.86 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 169.9 (C=O), 158.7 (C=O), 81.8 (C), 62.2 (CH_2), 57.6 (CH), 41.0 (CH_2), 27.9 (CH_3), 22.3 (CH_2), 10.7 (CH_3) ppm. HRMS (EI) found: [M^+], 229.1314, $C_{11}H_{19}NO_4$ requires [M^+], 229.1323; LRMS (EI): *m*/*z* (%) = 229 (2) [M^+], 128 (100).

***tert*-Butyl {2-[4-(Chlorophenyl)thio]ethyl}aminoacetate, HCl Salt (17a):** Potassium *tert*-butoxide (1.06 g, 9.4 mmol) was added to a stirred solution of 4-chlorothiophenol (1.77 g, 12.2 mmol) in *tert*-butyl alcohol (35 mL). After 10 min the oxazolidinone **16a** (1.73 g, 8.6 mmol) was added and the mixture was heated under reflux. After 22 h the solvent was evaporated and the residue was dissolved in Et_2O (30 mL) and HCl (25 mL, 0.5 M) was added. The mixture was filtered and dried ($MgSO_4$) to give, after recrystallisation from 2-propanol, the HCl salt of the amino ester **17a** (2.89 g, 92%) as needles; m.p. 128–129 °C. R_f = 0.43 [petrol/EtOAc (1:1)]. IR (neat): $\tilde{\nu}_{max}$ = 3380, 2985, 1735, 1655 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.40 (d, *J* = 8.5 Hz, 2 H, ArH), 7.27 (d, *J* = 8.5 Hz, 2 H, ArH), 3.79 (s, 2 H, CH_2), 3.54–3.51 (t, *J* = 8.0 Hz, 2 H, CH_2), 3.28–3.24 (t, *J* = 8.0 Hz, 2 H, CH_2), 1.46 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 165.1 (C=O), 133.4, (C), 132.4 (C), 131.7 (CH), 129.8 (CH), 85.1 (C), 48.3 (CH_2), 47.2 (CH_2), 29.5 (CH_2), 28.3 (CH_3) ppm. HRMS (ES) found: [M^+ – Cl], 302.0970, $C_{14}H_{21}ClNO_2S$ requires [M^+ – Cl], 302.0982. LRMS (ES): *m*/*z* (%) = 302 (88) [MH^+], 246 (100). $C_{14}H_{21}Cl_2NO_2S$ (337.07): calcd. C 49.71, H 6.26, N 4.14, Cl 20.96, S 9.48; found C 49.45, H 6.47, N 3.84, Cl 20.78, S 9.52.

***tert*-Butyl {2-[4-(Chlorophenyl)thio]ethyl}aminobutyrate, HCl Salt (17b):** Potassium *tert*-butoxide (2.88 g, 25.6 mmol) was added to a stirred solution of 4-chlorothiophenol (3.71 g, 25.6 mmol) in *tert*-butyl alcohol (110 mL). After 10 min the oxazolidinone **16b** (5.35 g, 23.3 mmol) was added and the mixture was heated under reflux. After 26 h the solvent was evaporated and the residue was dissolved in Et_2O (100 mL) and HCl (30 mL, 0.5 M) was added. The mixture was filtered and dried ($MgSO_4$) to give, after recrystallisation from 2-propanol, the HCl salt of the amino ester **17b** (6.05 g, 80%) as needles; m.p. 132–133 °C. R_f = 0.75 [petrol/EtOAc (1:1)]. IR (neat): $\tilde{\nu}_{max}$ = 3390, 2970, 2790, 1740, 1560 cm^{-1}. ^1H NMR (250 MHz, CD_3OD): δ = 7.47–7.38 (m, 2 H, ArH), 7.37–7.29 (m, 2 H, ArH), 3.95–3.88 (dd, *J* = 6.5, 5.0 Hz, 1 H, CH), 3.31–3.04 (m, 4 H, CH_2CH_2), 2.10–1.85 (m, 2 H, CH_2), 1.46 (s, 9 H, *t*Bu), 1.04–0.95 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (63 MHz, CD_3OD): δ = 169.0 (C=O), 134.4, (C), 133.8 (C), 133.0 (CH), 130.6 (CH), 85.9 (C), 62.7 (CH), 46.9 (CH_2), 30.5 (CH_2), 28.1 (CH_3), 24.0 (CH_2), 9.3 (CH_3) ppm. HRMS (ES) found: [M^+ – Cl], 330.1292, $C_{16}H_{25}ClNO_2S$ requires [M^+ – Cl], 330.1295; LRMS (ES): *m*/*z* (%) = 330 (37) [MH^+], 274 (100). $C_{16}H_{25}Cl_2NO_2S$ (365.10): calcd. C 52.46, H 6.88, N 3.82, Cl 19.35, S 8.75; found C 52.41, H 6.63, N 4.11, Cl 19.33, S 8.92.

{2-[4-(Chlorophenyl)thio]ethyl}aminoacetic Acid, HCl Salt (18a): Anhydrous HCl (100 mL, 4 M solution in dioxane) was added to the ester **17a** (6.29 g, 21 mmol) and the mixture was warmed to 50 °C. After 1 h the solvent was evaporated to give, after recrystallisation from 2-propanol, the amino acid **18a** (3.81 g, 65%) as needles; m.p. 197–198 °C. R_f = 0.24 [CH_2Cl_2/MeOH (4:1)]. IR (neat): $\tilde{\nu}_{max}$ = 2890, 2790, 1745, 1640 cm^{-1}. ^1H NMR (250 MHz, CD_3OD): δ = 7.25–7.19 (m, 2 H, ArH), 7.17–7.09 (m, 2 H, ArH), 3.72 (s, 2 H, CH_2), 3.10–3.00 (m, 4 H, CH_2CH_2) ppm. ^{13}C NMR (90 MHz, CD_3OD): δ = 169.1 (C=O), 134.9 (C), 134.1 (C), 133.5 (CH), 131.0 (CH), 48.7 (CH_2), 48.0 (CH_2), 31.0 (CH_2) ppm. HRMS (ES) found: [M^+ – Cl], 246.0356, $C_{10}H_{13}ClNO_2S$ requires [M^+ – Cl], 246.0351; LRMS (ES): *m*/*z* (%) = 246 (100) [MH^+]. $C_{10}H_{13}Cl_2NO_2S$ (281.00): calcd. C 42.56, H 4.64, N 4.96, Cl 25.13, S 11.36; found C 42.29, H 4.42, N 5.04, Cl 24.94, S 11.35.

{2-[4-(Chlorophenyl)thio]ethyl}aminobutyric Acid, HCl Salt (18b): Anhydrous HCl (80 mL, 4 M solution in dioxane) was added to the ester **17b** (3.05 g, 9 mmol) and the mixture was warmed to 50 °C. After 1 h the solvent was evaporated to give, after recrystallisation from 2-propanol, the amino acid **18b** (2.1 g, 81%) as needles; m.p. 191–192 °C. R_f = 0.42 [CH_2Cl_2/MeOH (4:1)]. IR (neat): $\tilde{\nu}_{max}$ = 2975, 2800, 1730, 1550 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): δ = 7.37–7.34 (m, 2 H, ArH), 7.28–7.25 (m, 2 H, ArH), 3.91 (dd, *J* = 11.5, 5.0 Hz, 1 H, CH), 3.25–3.10 (m, 4 H, CH_2CH_2), 1.99–1.85 (m, 2 H, CH_2), 0.94 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (90 MHz, CD_3OD): δ = 171.8 (C=O), 134.5 (C), 134.3 (C), 133.3 (CH), 131.0 (CH), 62.7 (CH), 47.5 (CH_2), 30.9 (CH_2), 24.3 (CH_2), 9.7 (CH_3) ppm. HRMS (ES) found: [M^+ – Cl], 274.0669, $C_{12}H_{17}ClNO_2S$ requires [M^+ – Cl], 274.0675. LRMS (ES): *m*/*z* (%) = 274 (100) [MH^+]. $C_{12}H_{17}Cl_2NO_2S$ (309.04): calcd. C 46.46, H 5.52, N 4.51, Cl 22.85, S 10.34; found C 46.34, H 5.52, N 4.67, Cl 22.62, S 10.32.

Methyl 3-(2-Methylaminoethyl)carbazole-9-carboxylate (19): 1-Chloroethyl chloroformate (0.07 mL, 0.6 mmol) was added to the amine **13** (164 mg, 0.6 mmol) in PhMe (15 mL) and the mixture was heated under reflux. After 16 h the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol/EtOAc (4:1), to give the intermediate carbamate, which was dissolved in MeOH (40 mL) and heated at 40 °C. After 2 d, the solvent was evaporated and the residue was purified by column chromatography, eluting with CH_2Cl_2/MeOH (4:1), to give the amine **19** (45 mg, 27%), recrystallised from petrol/CH_2Cl_2 as plates; m.p. 191–192 °C (dec.). R_f = 0.29 [CH_2Cl_2/MeOH (9:1)]. IR (neat): $\tilde{\nu}_{max}$ = 3050, 2950, 2770, 1735, 1655, 1605, 1580 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.0 Hz, 1 H, ArH), 8.04 (d, *J* = 8.0 Hz, 1 H, ArH), 7.80–7.69 (m, 2 H, ArH), 7.39–7.30 (m, 1 H, ArH), 7.25–7.16 (m, 2 H, ArH), 4.00 (s, 3 H, OCH_3), 3.35–3.13 (m, 4 H, CH_2CH_2), 2.67 (s, 3 H, NCH_3) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 152.7 (C=O), 138.4 (C), 137.2 (C), 131.2 (C), 127.5 (CH), 127.4 (CH), 126.4 (C), 125.4 (C), 123.4 (CH), 119.7 (2 CH), 116.5 (CH), 116.1 (CH), 53.5 (CH$_3$), 51.0 (CH$_2$), 33.2 (CH$_3$), 32.3 (CH$_2$) ppm. HRMS (ES) found: [MH$^+$], 283.1457, C$_{17}$H$_{19}$N$_2$O$_2$ requires [MH$^+$], 283.1447. LRMS (ES): *m*/*z* (%) = 283 (100) [MH$^+$], 252 (49).

Sodium Allylaminoacetate: To a stirred solution of ethyl allylaminoacetate[25] (1.48 g, 10.3 mmol) in THF (10 mL) and H$_2$O (10 mL) was added NaOH (0.41 g, 10.3 mmol). After 16 h the mixture was washed with petrol, then evaporated to give the title compound (1.27 g, 90%) as a solid; m.p. 237–238 °C (dec.). IR (neat): $\tilde{\nu}_{max}$ = 3310, 3075, 3005, 2815, 1635, 1580 cm^{-1}. ^{1}H NMR (250 MHz, D$_2$O): δ = 5.67 (ddt, *J* = 16.5, 10.5, 6.0 Hz, 1 H, CH=), 5.05–4.88 (m, 2 H, CH$_2$=), 3.01–2.90 (m, 4 H, 2 CH$_2$) ppm. ^{13}C NMR (63 MHz, D$_2$O): δ = 179.3 (C=O), 135.1 (CH), 117.0 (CH$_2$), 51.1 (CH$_2$), 50.4 (CH$_2$) ppm. HRMS (ES) found: [MNa$^+$], 160.0358, C$_5$H$_8$NO$_2$Na requires [MNa$^+$], 160.0350.

Ethyl 2-(Allylamino)butyrate: Allylamine (7.7 g, 135 mmol) and Et$_3$N (13.6 g, 135 mmol) in MeCN (100 mL) was added to ethyl 2-bromobutyrate (26.4 g, 135 mmol) and the mixture was heated under reflux. After 16 h saturated NaHCO$_3$ (100 mL) was added and the mixture was extracted with EtOAc (4 × 50 mL), dried (MgSO$_4$), filtered and the solvents evaporated. Purification by column chromatography, eluting with petrol/EtOAc (3:2), gave the amino ester (18.8 g, 82%) as an oil. R_f = 0.58 [petrol/EtOAc (1:1)]. IR (neat): $\tilde{\nu}_{max}$ = 3055, 2880, 1730, 1645 cm^{-1}. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 5.68 (ddt, *J* = 16.5, 10.5, 5.0, = Hz, 1 HCH), 5.06–4.85 (m, 2 H, H$_2$C=), 4.01 (q, *J* = 7.0 Hz, 2 H, OCH$_2$), 3.15–2.88 (m, 3 H, CH$_2$ and CH), 1.56–1.41 (m, 2 H, CH$_2$), 1.11 (t, *J* = 7.0 Hz, 3 H, CH$_3$), 0.77 (t, *J* = 7.5 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 174.6 (C=O), 136.4 (CH), 115.4 (CH$_2$), 61.4 (CH), 59.8 (CH$_2$), 50.3 (CH$_2$), 26.2 (CH$_2$), 13.9 (CH$_3$), 9.6 (CH$_3$) ppm. HRMS (EI) found: [M$^+$], 171.1259, C$_9$H$_{17}$NO$_2$ requires [M$^+$], 171.1259; LRMS (ES): *m*/*z* (%) = 171 (10) [M$^+$], 99 (100).

Sodium 2-(Allylamino)butyrate: NaOH (1.4 g, 35.5 mmol) was added to ethyl 2-(allylamino)butyrate (6.1 g, 35.5 mmol) in THF (10 mL) and H$_2$O (10 mL). After 16 h the solvent was evaporated to give the title compound (5.2 g, 89%) as a solid; 218–219 °C (dec.). IR (neat): $\tilde{\nu}_{max}$ = 3305, 3075, 2875, 2805, 1640, 1575 cm^{-1}. ^{1}H NMR (250 MHz, D$_2$O): δ = 5.81 (ddt, *J* = 17.0, 10.5, 6.5 Hz, 1 H, =CH), 5.41–5.27 (m, 2 H, H$_2$C=), 3.52–3.28 (m, 3 H, 3 × CH), 1.84–1.58 (m, 2 H, CH$_2$), 0.87 (t, *J* = 7.5 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (90 MHz, D$_2$O): δ = 182.5 (C=O), 135.2 (CH), 117.0 (CH$_2$), 64.1 (CH), 49.6 (CH$_2$), 25.9 (CH$_2$), 9.6 (CH$_3$) ppm. HRMS (ES) found: [MNa$^+$], 188.0665, C$_7$H$_{12}$NO$_2$Na$_2$ requires [MNa$^+$], 188.0663; LRMS (ES): *m*/*z* (%) = 188 (100) [MNa$^+$], 166 (40) [MH].

6-Methyl 1-Allyl-2,3,3a,4,5,10c-hexahydro-1*H*-pyrrolo[3,2-*c*]carbazole-6-carboxylate (20): Sodium (allylamino)acetate, prepared as described above, (824 mg, 6.0 mmol) and camphorsulfonic acid (1.5 g, 6.0 mmol) was added to the aldehyde **7** (155 mg, 0.6 mmol) in toluene (50 mL) and the mixture was heated under reflux. After 5 d, saturated NaHCO$_3$ (20 mL) was added and the mixture was extracted with CH$_2$Cl$_2$ (4 × 20 mL), dried (MgSO$_4$), filtered and the solvents evaporated. Purification by column chromatography, eluting with CH$_2$Cl$_2$/MeOH (96:4), gave the amine **20** (78 mg, 42%) as an oil. R_f = 0.58 [CH$_2$Cl$_2$/MeOH (96:4)]. IR (neat): $\tilde{\nu}_{max}$ = 3070, 2950, 1730, 1605 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.13–8.09 (m, 1 H, ArH), 7.58–7.54 (m, 1 H, ArH), 7.26–7.19 (m, 2 H, ArH), 5.93–5.84 (m, 1 H, =CH), 5.21 (dd, *J* = 17.0, 1.0 Hz, 1 H, HC=), 5.05 (d, *J* = 10.5 Hz, 1 H, HC=), 4.01 (s, 3 H, OCH$_3$), 3.78–3.73 (m, 1 H, CH), 3.54 (d, *J* = 5.5 Hz, 1 H, CH), 3.22 (ddd, *J* = 18.5, 5.5, 4.0 Hz, 1 H, CH), 3.18–3.12 (m, 1 H, CH), 3.01 (dd, *J* = 12.5, 8.0 Hz, 1 H, CH), 2.94–2.85 (m, 1 H, CH), 2.36–2.29 (m, 1 H, CH), 2.29–2.22 (m, 1 H, CH), 2.16–2.04 (m, 2 H, 2 CH), 1.87–1.80 (m, 1 H, CH), 1.63–1.56 (m, 1 H, CH) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = 152.6 (C=O), 138.2 (C), 136.7 (CH), 136.0 (C), 130.2 (C), 123.4 (CH), 122.8 (CH), 118.6 (CH), 116.5 (CH$_2$), 116.4 (C), 115.4 (CH), 60.1 (CH), 58.9 (CH$_2$), 53.3 (CH$_3$), 52.3 (CH$_2$), 36.3 (CH), 28.6 (CH$_2$), 27.6 (CH$_2$), 24.9 (CH$_2$) ppm. HRMS (ES) found: [MH$^+$], 311.1755, C$_{19}$H$_{23}$N$_2$O$_2$ requires [MH$^+$], 311.1760. LRMS (ES): *m*/*z* (%) = 311 (100) [MH$^+$].

Methyl 3-(Allylaminomethyl)-2-but-3-enylindole-1-carboxylate (21): R_f = 0.40 [CH$_2$Cl$_2$/MeOH (95:5)]. IR (neat): $\tilde{\nu}_{max}$ = 3340, 3070, 2930, 2855, 1735, 1640, 1605, 1575 cm^{-1}. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 8.02–7.93 (m, 1 H, ArH), 7.55–7.46 (m, 1 H, ArH), 7.22–7.10 (m, 2 H, ArH), 5.95–5.69 (m, 2 H, 2 × HC=), 5.19–4.85 (m, 4 H, 2 × =CH$_2$), 3.95 (s, 3 H, OCH$_3$), 3.76 (s, 2 H, CH$_2$), 3.25–3.19 (m, 2 H, CH$_2$), 3.12–3.03 (m, 2 H, CH$_2$), 2.30 (q, *J* = 7.5 Hz, 2 H, CH$_2$) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 152.4 (C=O), 138.1 (C), 137.8 (CH), 137.0 (CH), 135.8 (C), 129.9 (C), 124.0 (CH), 123.0 (CH), 118.5 (CH), 118.0 (C), 116.1 (CH$_2$), 115.7 (CH), 115.3 (CH$_2$), 53.5 (CH$_3$), 52.1 (CH$_2$), 42.5 (CH$_2$), 34.3 (CH$_2$), 26.4 (CH$_2$) ppm. HRMS (EI) found: [M$^+$], 298.1681, C$_{18}$H$_{22}$N$_2$O$_2$ requires [M$^+$], 298.1669; LRMS (EI): *m*/*z* (%) = 299 (9) [MH$^+$], 298 (44), 241 (100).

6-Methyl 1-Allyl-2-ethyl-2,3,3a,4,5,10c-hexahydro-1*H*-pyrrolo[3,2-*c*]carbazole-6-carboxylate (22): Sodium 2-(allylamino)butyrate, prepared as described above, (1.11 g, 6.7 mmol) and *p*-toluenesulfonic acid (1.03 g, 5.4 mmol) was added to a stirred solution of the aldehyde **7** (173 mg, 0.67 mmol) in toluene (50 mL) and the mixture was heated under reflux. After 16 h, the mixture was filtered through Celite, washed with CH$_2$Cl$_2$ (25 mL) and the solvents evaporated. To this mixture at room temperature in CH$_2$Cl$_2$ (25 mL) was added pyridine (0.06 mL, 0.67 mmol) and methyl chloroformate (0.05 mL, 0.67 mmol). After 16 h the solvent was evaporated and the residue was purified by column chromatography, eluting with CH$_2$Cl$_2$/MeOH (9:1), to give the amine **22** (42 mg, 19%) as an oil. R_f = 0.23 [CH$_2$Cl$_2$/MeOH (95:5)]. IR (neat): $\tilde{\nu}_{max}$ = 3075, 2930, 2855, 1740, 1640, 1605 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.04–8.01 (m, 1 H, ArH), 7.60–7.54 (m, 1 H, ArH), 7.20–7.15 (m, 2 H, ArH), 5.72 (ddt, *J* = 17, 10, 6 Hz, 1 H, =CH), 5.03–4.95 (m, 1 H, =CH), 4.93–4.86 (m, 1 H, =CH), 4.22 (d, *J* = 5 Hz, 1 H, NCH), 3.94 (s, 3 H, OMe), 3.28 (dd, *J* = 14, 5.5 Hz, 1 H, CH), 3.13 (dt, *J* = 18, 4.5 Hz, 1 H, CH), 3.03 (dd, *J* = 14, 6.5 Hz, 1 H, CH), 3.00–2.92 (m, 1 H, CH), 2.86–2.72 (m, 1 H, CH), 2.30–2.22 (m, 1 H, CH), 1.84–1.58 (m, 5 H, 5 CH), 1.31–1.20 (m, 1 H, CH), 0.81 (t, *J* = 7.5 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 152.2 (C), 140.6 (C), 135.5 (C), 128.7 (CH), 128.3 (C), 125.1 (CH), 124.8 (CH), 123.7 (C), 120.5 (CH), 115.3 (CH), 109.1 (CH$_2$), 68.1 (CH), 61.6 (CH), 56.0 (CH$_2$), 53.9 (CH$_3$), 36.6 (CH$_2$), 36.2 (CH), 26.1 (CH$_2$), 25.4 (CH$_2$), 24.3 (CH$_2$), 11.0 (CH$_3$) ppm. HRMS (ES) found: [M$^+$], 338.2002, C$_{21}$H$_{26}$N$_2$O$_2$ requires [M$^+$], 338.1994; LRMS (ES): *m*/*z* (%) = 339 (100) [MH$^+$], 242 (61).

Vinyl Sulfone 25: Grubbs' 2nd generation catalyst (73 mg, 5 mol-%) was added to the alkene **7** (442 mg, 1.7 mmol) and phenyl vinyl sulfone (577 mg, 3.4 mmol) in CH$_2$Cl$_2$ (25 mL). The mixture was heated under reflux for 21 h, then another portion of the catalyst (73 mg, 5 mol-%) was added and heating continued for a further 1 h. The solvent was evaporated and the mixture was purified by column chromatography, eluting with petrol/EtOAc (7:3), to give the vinyl sulfone **25** (294 mg, 43%) as an oil; R_f = 0.16 [petrol/EtOAc (7:3)]. IR (neat): $\tilde{\nu}_{max}$ = 3055, 2955, 2920, 2845, 1750, 1660, 1555, 1385, 1150 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 10.19 (s, 1 H, CHO), 8.19–8.10 (m, 1 H, ArH), 7.95–7.87 (m, 1 H, ArH), 7.78–7.70 (m, 2 H, ArH), 7.55–7.35 (m, 3 H, ArH), 7.31–7.23 (m, 2 H, ArH), 6.95 (dt, J = 15.0, 7.5 Hz, 1 H, =CH), 6.31 (d, J = 15.5 Hz, 1 H, =CH), 4.04 (s, 3 H, OCH_3), 3.55–3.45 (m, 2 H, CH_2), 2.67–2.53 (m, 2 H, CH_2) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 185.4 (C=O), 151.7 (C=O), 149.4 (C), 144.1 (CH), 140.2 (C), 135.3 (C), 133.4 (CH), 132.0 (CH), 129.3 (CH), 127.6 (CH), 126.1 (C), 156.3 (CH), 124.8 (CH), 120.8 (CH), 118.8 (C), 115.5 (CH), 54.6 (CH_3), 31.8 (CH_2), 24.8 (CH_2) ppm. HRMS (ES) found: [MNa^+], 420.0863, $C_{21}H_{19}NO_5NaS$ requires [MNa^+], 420.0882. LRMS (ES): m/z (%) = 420 (100) [MNa^+].

Cycloadduct Sulfone 26: Sodium (allylamino)acetate, prepared as described above, (72 mg, 0.52 mmol) and camphorsulfonic acid (131 mg, 0.52 mmol) was added to the aldehyde **25** (104 mg, 0.26 mmol) in toluene (20 mL) and the mixture was heated under reflux. After 16 h, the solvent was evaporated and the mixture was purified by column chromatography, eluting with petrol/EtOAc (1:1), to give the amine **26** (86 mg, 73%) as an oil. R_f = 0.36 [petrol/EtOAc (1:1)]. IR (neat): $\tilde{\nu}_{max}$ = 3065, 2960, 2920, 2860, 1735, 1605, 1460, 1140 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.03–7.99 (m, 1 H, ArH), 7.89–7.85 (m, 2 H, ArH), 7.62–7.58 (m, 1 H, ArH), 7.54–7.47 (m, 3 H, ArH), 7.20–7.14 (m, 2 H, ArH), 5.79–5.69 (m, 1 H, =CH), 5.16 (dd, J = 17.0, 0.5 Hz, 1 H, HC=), 5.04–4.98 (m, 1 H, HC=), 3.93 (s, 3 H, OCH_3), 3.80 (d, J = 5.0 Hz, 1 H, CH), 3.60 (dd, J = 13.0, 5.5 Hz, 1 H, CH), 3.40–3.35 (m, 1 H, CH), 3.20 (t, J = 10.0 Hz, 1 H, CH), 3.12–3.02 (m, 2 H, $2\times$CH), 2.86–2.76 (m, 2 H, $2\times$CH), 2.74–2.68 (m, 1 H, CH), 2.01–1.91 (m, 1 H, CH), 1.73–1.67 (m, 1 H, CH) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 152.4 (C=O), 138.6, (C), 137.5 (C), 135.8 (CH), 135.7 (C), 133.8 (CH), 129.7 (C), 129.4 (CH), 128.1 (CH), 123.8 (CH), 122.9 (CH), 118.8 (CH), 117.4 (C, CH_2), 114.9 (CH), 66.5 (CH), 59.9 (CH), 58.0 (CH_2), 53.5 (CH_3), 52.2 (CH_2), 38.4 (CH), 26.2 (CH_2), 24.2 (CH_2) ppm. HRMS (ES) found: [MH^+], 451.1677, $C_{25}H_{27}N_2O_4S$ requires [MH^+], 451.1692. LRMS (ES): m/z (%) = 451 (100) [MH^+].

6-Methyl 2,3,3a,4,5,10c-Hexahydro-1*H*-pyrrolo[3,2-*c*]carbazole-6-carboxylate (2): Bis(dibenzylideneacetone)palladium (32 mg, 0.05 mmol) was added to 1,4-bis(diphenylphosphanyl)butane (24 mg, 0.05 mmol) in dry THF (1 mL) under nitrogen at room temperature. After 15 min, a mixture of the amine **20** (70 mg, 0.23 mmol) in dry THF (2 mL) and thiosalicylic acid (42 mg, 0.27 mmol) was added. After 3 h, saturated $NaHCO_3$ (10 mL) was added and the mixture was extracted with EtOAc (3×10 mL), dried ($MgSO_4$), filtered and the solvents evaporated. Purification by column chromatography, eluting with CH_2Cl_2/MeOH (9:1), gave the amine **2** (25 mg, 40%) as a solid. R_f = 0.19 [CH_2Cl_2/MeOH (9:1)]. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.10–8.06 (m, 1 H, ArH), 7.64–7.60 (m, 1 H, ArH), 7.28–7.20 (m, 2 H, ArH), 4.15 (d, J = 6.0 Hz, 1 H, CH), 4.01 (s, 3 H, OCH_3), 3.16–3.07 (m, 2 H, $2\times$CH), 3.03–2.96 (m, 1 H, CH), 2.92–2.84 (m, 1 H, CH), 2.42–2.34 (m, 1 H, CH), 2.16–2.03 (m, 2 H, NH & CH), 1.90–1.83 (m, 1 H, CH), 1.71–1.62 (m, 1 H, CH), 1.62–1.54 (m, 1 H, CH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.6 (C=O), 137.0 (C), 135.9 (C), 129.4 (C), 123.8 (CH), 123.0 (CH), 118.6 (CH), 117.8 (C), 115.3 (CH), 54.7 (CH), 53.4 (CH_3), 46.1 (CH_2), 37.2 (CH), 30.9 (CH_2), 26.3 (CH_2), 24.1 (CH_2) ppm. HRMS (ES) found: [MH^+], 271.1439, $C_{16}H_{19}N_2O_2$ requires [MH^+], 271.1447; data matches that in the literature.[7]

Supporting Information (see also the footnote on the first page of this article): Copies of NMR spectra for compounds **9**–**11**, **14a**, **14b**, **15a**, **15b**, **16b**, **20**–**22**, **25**, **26** and **2**.

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