Synthesis of 3,4-Bridged Indoles by Photocyclisation Reactions. Part 1. Photocyclisation of Halogenoacetyl Tryptophan Derivatives

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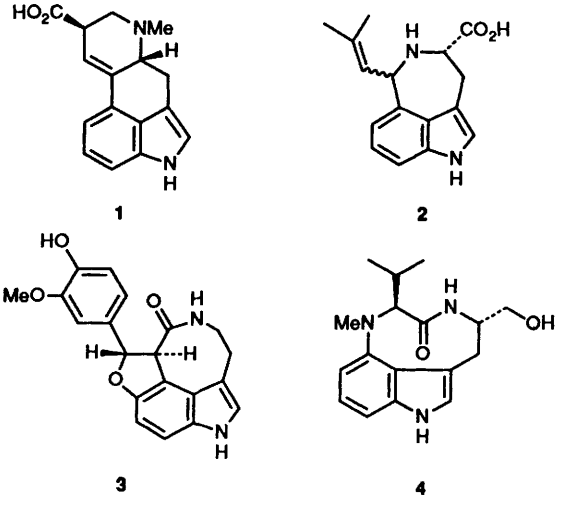
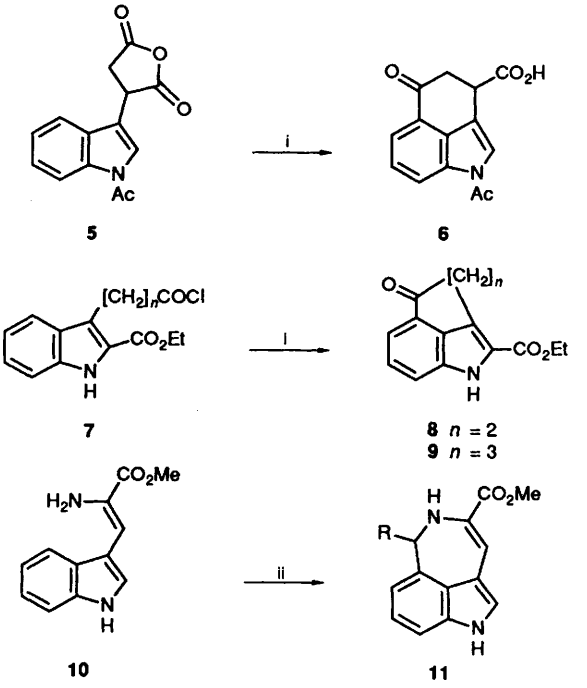
Although irradiation of *N*-chloroacetyltryptophan results in a poor yield of photocyclisation to the indole 4-position due to competing cyclisation to C-2, the photocyclisation of (dichloroacetyl)tryptophan derivatives gives, after addition of a nucleophile in work-up, 7-substituted pyrrolobenzazocines in good yield and with *trans*-stereospecificity. *N*-(Trichloroacetyl)tryptophan derivatives also undergo photocyclisation to give 3,4-bridged indoles. The structures of the azocinoindoles **13**, **21**, **22** and **35**, and the azepinoindole **15** were confirmed by X-ray crystallography. In one case the preparation of a cycloalka[*c,d*]indole was possible by the irradiation of the α-chloro amide of an indol-3-yl alkanoic acid.

Of the naturally occurring indoles, those in which the indole 3-position is bridged to the 4-position ([*c,d*]-fused indoles) are among the most interesting in terms of biological activity. Examples include the well known lysergic acid **1**,[1] as well as clavicipitic acid **2**,[2] serotobenine **3**,[3] and indolactam V **4**,[4] where the indole is bridged by 6-, 7-, 8- and 9-membered rings, respectively.



1 **2** **3** **4**

In Nature, compounds such as **1** and **2** are invariably biosynthesized from tryptophan, with an isoprene unit being introduced in the indole 4-position by the enzyme dimethylallylpyrophosphate tryptophan dimethylallyl transferase. This *direct* functionalisation of the indole 4-position is extremely difficult to carry out in the laboratory although there are a few examples. Hence, treatment of the anhydride of *N*-acetylindole-3-succinic acid, compound **5**, with aluminium chloride to give the tetrahydrobenz[*c,d*]indole **6**, a compound related to Uhle's ketone, has been described.[5] Subsequently it was shown that cyclisations of this sort generally took place at the indole 2-position unless it was blocked, and therefore the analogous indole **8** ($n = 2$) could only be derived from the 2-ethoxycarbonyl derivative of indole-3-propionyl chloride, compound **7** ($n = 2$), albeit in only 24% yield.[6] Under the same conditions, the cycloheptaindole **9** ($n = 3$) was obtained in 73% yield, whilst the 8-membered ring ($n = 4$) was not formed at all. More recently, the condensation of didehydrotryptophan methyl ester **10** with various aldehydes in the presence of camphorsulfonic acid (CSA) or boron trifluoride–diethyl ether has been reported to yield the 4-cyclised products **11** (21–45%).[7] However, despite the limited success of the above Friedel–Crafts-type cyclisations in indoles, it is still more common to carry out such cyclisations on indolines,[8] and then to oxidise the 5-membered ring at a later stage. The alternative, commonly used laboratory approach involves the linking together of existing functionality in both the 3- and 4-position of the indole ring, such 3,4-disubstituted indoles often being prepared by a ring synthesis (of the 4-substituted compound) such as the Leimgruber–Batchko method,[9] followed by an electrophilic substitution to introduce the 3-substituent.



5 **6** **7** **8** $n = 2$ **9** $n = 3$ **10** **11**

Reagents: i, $AlCl_3$; ii, RCHO, CSA or $BF_3{\cdot}Et_2O$

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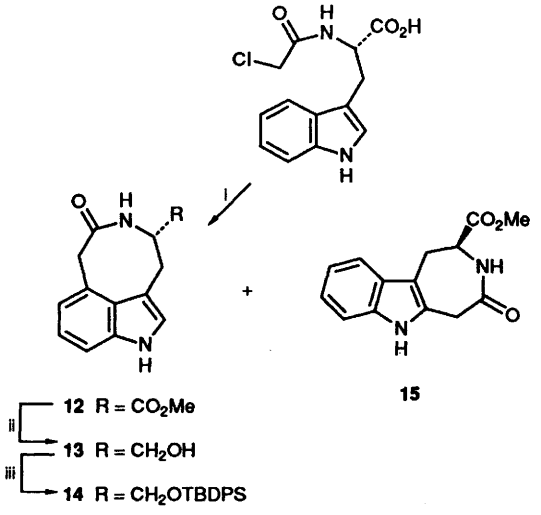
We have now adapted a photochemically induced ring closure of simple tryptophan derivatives to the synthesis of 3,4-bridged indoles. The results described in full herein constitute a useful extension of classic tryptophan chemistry, which has long been used to prepare the well known 2,3-fused indoles such as β-carbolines, to the much more difficult 3,4-fused systems.[10]

Results and Discussion

Our photochemical approach is based on an attempted photoreduction of (chloroacetyl)tryptophan,[11] which resulted in an unusual cyclisation to the indole 4-position to give, after esterification, compound **12**. Although originally presented as something of a curiosity, the 'Witkop cyclisation' has subsequently been used on a number of indole-derived substrates,[12] as well as various phenethylamine derivatives.[13] Such cyclisations are also relevant to the photochemistry of some tryptophan-containing peptides.[14] The mechanism is discussed in detail in the following paper.



Scheme 1 *Reagents and conditions:* i, *hv*, water; followed by CH_2N_2, Et_2O–MeOH; ii, $NaBH_4$, EtOH; iii, Bu^tPh_2SiCl (TBDPSCl), imidazole, DMF

Our own attempts to carry out the original photochemical cyclisation,[11] however, were disappointing. Thus, irradiation of *N*-(chloroacetyl)tryptophan at 254 nm in aqueous neutral solution, followed by esterification of the crude product with diazomethane, gave the desired pyrrolobenzazocine **12** in poor yield (10–25% over numerous runs), owing in part to competing formation of the 2,3-fused isomer **15**, formed by cyclisation to the indole 2-position (Scheme 1). The structure of compound **15** was confirmed by X-ray crystallography (Fig. 1) as was that of the desired bridged product by an X-ray analysis of the

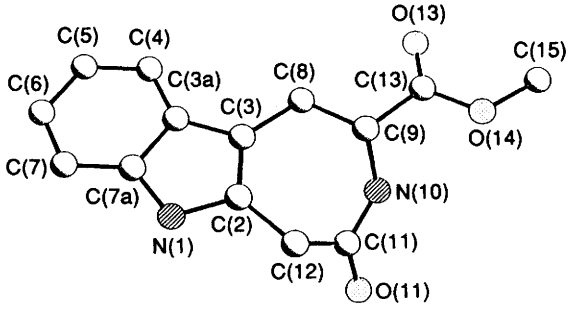


Fig. 1 X-Ray molecular structure of methyl 1,2,3,4,5,6-hexahydro-4-oxoazepino[4,5-*b*]indole-2-carboxylate **15** showing crystallographic numbering

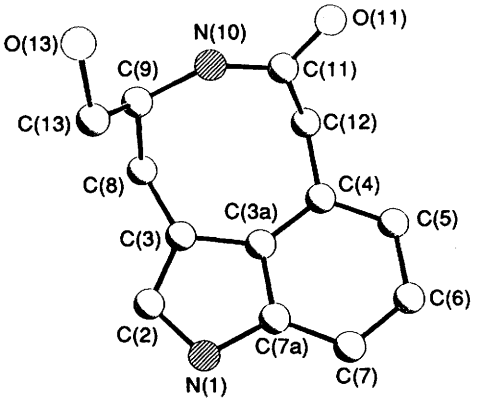
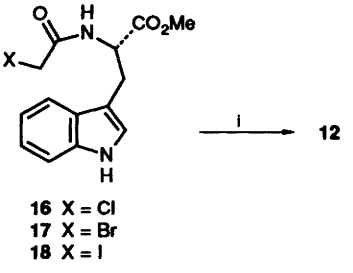


Fig. 2 X-Ray molecular structure of 1,3,4,5,6,7-hexahydro-4-hydroxymethyl-6-oxopyrrolo[4,3,2-*fg*][3]benzazocine **13** showing crystallographic numbering

crystalline alcohol **13** (Fig. 2) derived by sodium borohydride reduction. No mention was made of this alternative cyclisation product in the original paper, and it was only in the ensuing work [12a] that such a possibility was acknowledged, even though in our hands it accounted for considerable quantities of cyclised material.

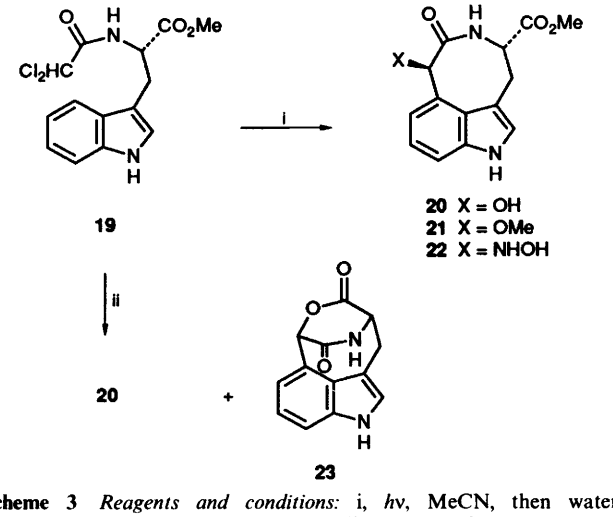
Therefore in an attempt to increase the yield of the required cyclisation product **12** we investigated the effect of solvent, irradiation wavelength, and the nature of the halogen 'leaving group'. The combination of switching to an organic solvent (acetonitrile) and irradiating (254 nm) the methyl ester **16** in place of the acid resulted in a slight increase in yield of the cyclised product **12** (34%). Irradiation at 350 nm led only to the recovery of starting material. The effect of 'leaving group' was briefly investigated by studying the irradiation of *N*-(bromoacetyl)- and -(iodoacetyl)-tryptophan **17** and **18** (Scheme 2). Monitoring of the reaction by HPLC showed that the chloro and bromo compounds reacted at a similar rate to give similar amounts of the desired product **12**, although the alternative cyclisation product **15** was more prominent in the reaction mixture from the chloroacetyl precursor **16**. The iodoacetyl compound, however, decomposed at a slower rate and gave rise to a number of additional, unidentified products. This may be attributed to the ease with which the carbon–iodine bond undergoes homolysis on irradiation.



Scheme 2 *Reagents and conditions:* i, *hv*, MeCN

The disappointing yields of the desired 3,4-bridged indoles obtained from the above (halogenoacetyl)tryptophan derivatives, coupled with the difficulties associated with functionalisation of the 7-position in the ester **12** or the protected alcohol **14** for further elaboration was a severe limitation. Therefore, the use of (dichloroacetyl)tryptophan derivatives as precursors was investigated, where the additional halogen would provide built-in functionality for the new ring. Thus, irradiation of (−)-(dichloroacetyl)tryptophan methyl ester **19** at 254 nm in acetonitrile gave, after chromatography, the 7-hydroxypyrrolo[4.3.2-*fg*][3]benzazocine **20** (58%) (Scheme 3), a major improvement in yield of photocyclised material. Alcohol **20** presumably arises by hydrolysis of the initially formed 7-chloro

derivative during the work-up/chromatography. Indeed, when the photolysis reaction mixture was worked up in the presence of other nucleophiles such as methanol or hydroxylamine, the corresponding 7-substituted pyrrolobenzazocines **21** (63%) and **22** (51%) were formed (Scheme 3). In all cases the yields were better than those obtained from the monochloro derivative and no evidence of competing cyclisation to the indole 2-position was found. The increased yields observed with the dichloro amides may be attributable to the higher selectivity of the chloroacetamido radical as opposed to the unsubstituted acetamido radical. The stabilising effect of chloride is reflected both in the C–H bond energies (D°_{298}/kcal mol^{-1})* of methane (105. 1), chloromethane (100.9), and in the heats of formation ($\Delta H^{\circ}_{f(298)}$/kcal mol^{-1}) of the methyl (35.1), dichloromethyl (24.1), and trichloromethyl (19.0) radicals.[15]



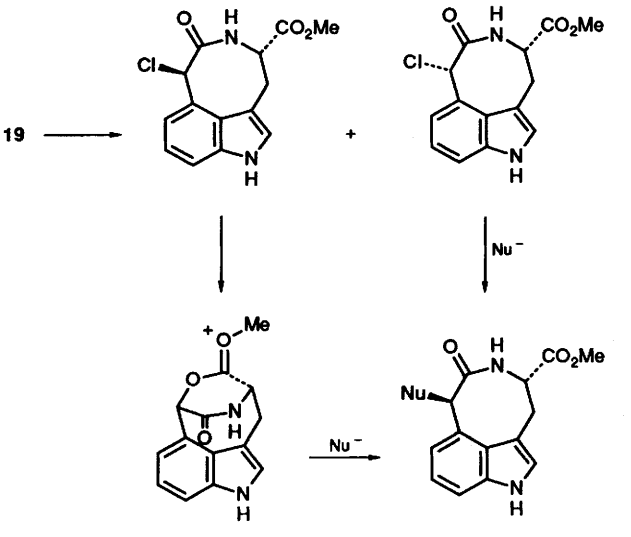
Scheme 3 *Reagents and conditions:* i, *hν*, MeCN, then water (chromatography), MeOH, or NH_2OH; ii, *hν*, aq. MeCN

The reaction also exhibits a remarkable degree of asymmetric induction in that the 7-substituent is exclusively *trans* to the ester group at C-4, the structures **21** and **22** being confirmed by X-ray crystallography (Figs. 3 and 4). We assume that the reaction proceeds with initial formation of a 7-chloro species with no stereochemical bias. This would be consistent with the observation that photocyclisation of AlaTrp gives a 1:1 mixture of diastereoisomeric 7-methylpyrrolobenzazocines,[14b] and with our results for the irradiation of compound **19** in aqueous solution which gave a ~1:1 mixture of 7-hydroxy isomers, the *cis*-isomer spontaneously cyclising to give the lactone **23** (Scheme 3). In the absence of a nucleophile *during* the irradiation, the observed *trans*-stereochemistry must then originate from the addition of a nucleophile during work-up. One possible explanation is shown in Scheme 4, and involves participation of the ester oxygen. Thus of the two possible chlorides (presumably formed in 1:1 ratio), the *trans*-chloride is displaced *in situ* by internal attack of the ester oxygen, and the resulting intermediate as well as the remaining *cis*-chloride are displaced during work-up by the external nucleophile, to give exclusively the *trans*-isomer product.

Evidence for the ease with which the internal displacement of the *trans*-chloride in these bridged indoles comes from the photocyclisation reaction of *N*-(dichloroacetyl)tryptophanol **24** which gave, after work-up with aq. sodium azide, the bridged ether **25** together with the *trans*-azide **26** (Scheme 5) albeit in modest yield due to difficulties with their isolation. When the tryptophanol hydroxy group was protected as its *tert*-butyldimethylsilyl (TBDMS) ether, no intramolecular reaction is possible and hence irradiation of the silyl ether **27** followed by addition of azide gave the *trans*-azide **28** in 36% yield. Deprotection of the silyl ether **28** gave the alcohol **26**. These results are consistent with the proposed mechanism.

Bearing in mind the previous discussion about the mechanism of the photocyclisation, and the effect of additional chloride

* 1 cal = 4.184 J.



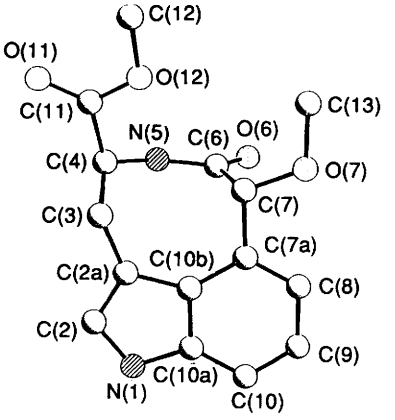


Fig. 3 X-Ray molecular structure of methyl 1,3,4,5,6,7-hexahydro-7-methoxy-6-oxopyrrolo[4,3,2-*fg*][3]benzazocine-4-carboxylate **21** showing crystallographic numbering

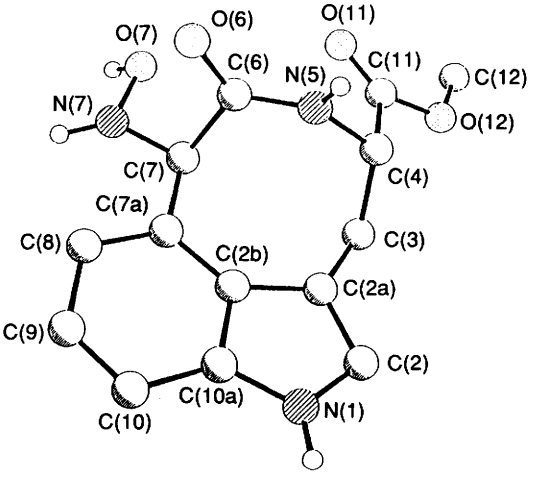
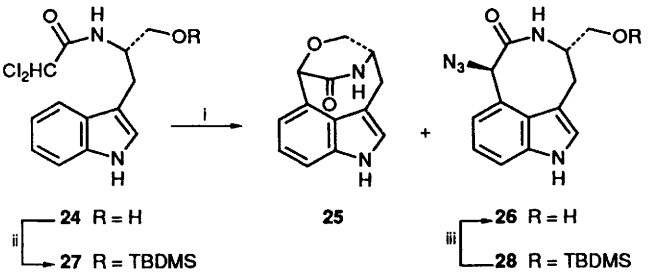
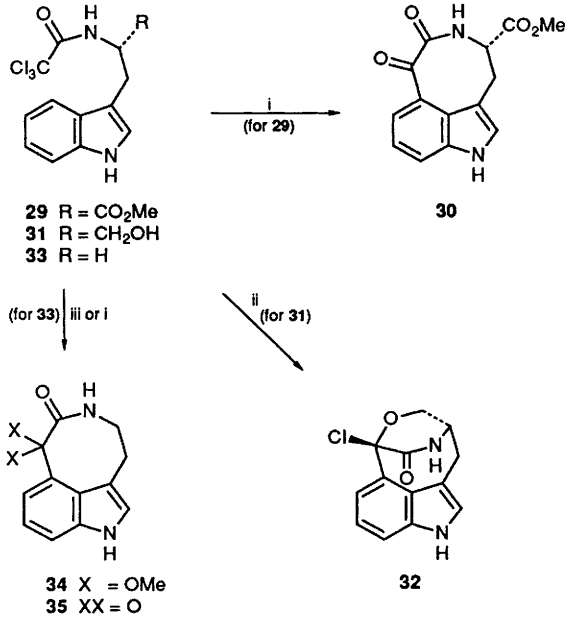


Fig. 4 X-Ray molecular structure of methyl 1,3,4,5,6,7-hexahydro-7-hydroxyamino-6-oxopyrrolo[4,3,2-*fg*][3]benzazocine-4-carboxylate **22** showing crystallographic numbering



Scheme 5 *Reagents and conditions:* i, *hv*, MeCN, then NaN_3; ii, TBDMSCl, imidazole, DMF; iii, AcOH, aq. THF, heat

atoms, the photocyclisation of *N*-(trichloroacetyl)tryptophan derivatives was expected to give even better yields of 4-cyclised products. Indeed, irradiation of the trichloroacetyl methyl ester **29** in wet acetonitrile gave the cyclic keto amide **30** (Scheme 6) in high yield, apparently by way of 7,7-dichloro- and 7-chloro-7-hydroxy intermediates. When the corresponding tryptophanol **31** was irradiated the cyclic chloro ether **32** was the only isolated product. Since one of two chlorine substituents in the first formed photocyclisation product is necessarily *trans* to the internal oxygen nucleophile it is readily displaced. Not surprisingly, the remaining chlorine could not be displaced for steric reasons.



Scheme 6 *Reagents and conditions:* i, *hv*, aq. MeCN; ii, *hv*, MeCN; iii, *hv*, MeCN, MeOH

The simple photocyclisation of *N*-(trichloroacetyl)tryptophan methyl ester was also extended to the corresponding tryptamine derivative **33**. When the irradiation was carried out in methanolic acetonitrile the major product (42%) was the dimethoxyazocinoindole **34** together with 12% of the keto amide **35** (Scheme 6). When the photocyclisation was carried out in aqueous acetonitrile, keto amide **35** was the sole product (64%). The structure of compound **35** was confirmed by X-ray crystallography (Fig. 5) which showed that the ketone carbonyl is twisted well out of the plane of the benzene ring.

We have also shown that the reaction tolerates an alkyl group at the reaction centre, and have extended the method to the preparation of azocinoindoles **38**/**39** related to serotobenine **3**. Acylation of tryptophan methyl ester with 2-chloro-3-phenylpropionyl chloride **36**, prepared from hydrocinnamic acid, gave the chloro amide **37**, irradiation of which gave a 1:3

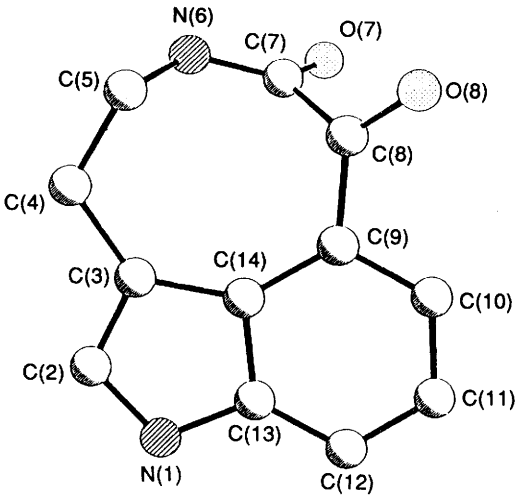
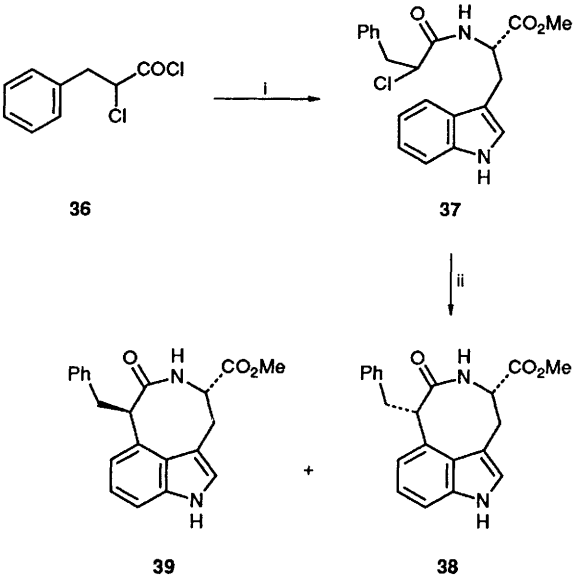


Fig. 5 X-Ray molecular structure of 1,3,4,5,6,7-hexahydro-6,7-dioxopyrrolo[4,3,2-*fg*][3]benzazocine **35** showing crystallographic numbering

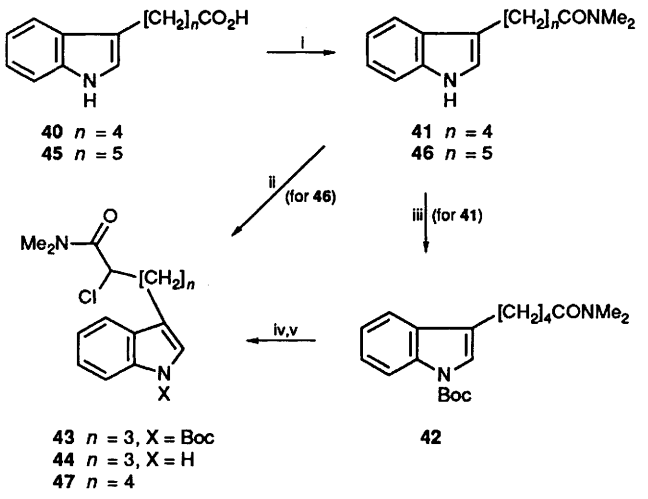
mixture of the photocyclised products (47% total) with the *trans*-diastereoisomer **39** predominating (Scheme 7).

The α-chloro amide is a key feature in all of the above photocyclisation reactions, and since these all derive from tryptophan the nitrogen of the amide necessarily forms part of the new ring. However, if the chloro amide were 'reversed,' then photocyclisation would lead to a carboxylic bridged indole



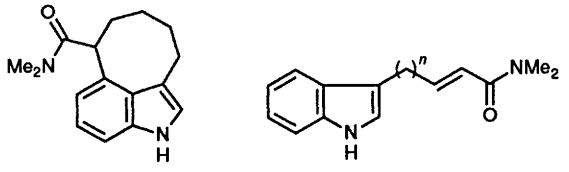
Scheme 7 *Reagents and conditions:* i, TrpOMe, $NaHCO_3$, aq. MeOH; ii, *hv*, MeCN

bearing an amide substituent. This possibility was investigated by the synthesis of two such precursors, the α-chloro amides **44** and **47**. The starting indole-3-alkanoic acids **40** and **45** were easily prepared by reaction of indole with the appropriate lactone in the presence of alkali,[16] and subsequently converted into the corresponding dimethyl amides **41**/**46**. In the case of the hexanamide **46** it was possible to chlorinate the dianion, formed by addition of lithium diisopropylamide (LDA) (2 mol equiv.) to give the desired α-chloro amide **47** directly. However, the dianion reaction on the pentanamide **41** proved troublesome and therefore the indole NH was protected as its *tert*-butoxycarbonyl (BOC) derivative **42**. Formation of the anion and chlorination then proceeded smoothly to give compound **43**, and the BOC group was cleaved in acid to give the required α-chloro amide **44** (Scheme 8).



Scheme 8 *Reagents and conditions:* i, Bu^tO_2CCl, Et_3N, Me_2NH; ii, LDA, THF, 0 °C, then CCl_4; iii, $(Boc)_2O$, DMAP, MeCN; iv, LICA, THF, −78 °C, then CCl_4; v, TFA, CH_2Cl_2.

Irradiation of the exo-amide **47** did indeed result in the desired photocyclisation and the cyclo-octaindole **48** was formed, albeit in poor yield (13%). The cyclised product was accompanied by the α,β-unsaturated amide **49**, formed by photoelimination of HCl. Attempts to prepare the cyclohepta-indole analogue of compound **48** by photocyclisation of the chloroamide **44** were unsuccessful, with the elimination product **50** being the only observed product (57% yield).



Thus a variety of functionalised tricyclic indoles, in which the 3- and 4-position are bridged by an 8-membered nitrogen-containing ring, can be prepared from tryptophan methyl ester in two simple steps—acylation, and photocyclisation with nucleophilic work-up. The extension of this reaction to tryptophol derivatives, and its application in the synthesis of the tumour-promoter indolactam V, are described in the following papers.

Experimental

General.—Commercially available solvents and reagents were used throughout without further purification, except for those detailed below which were purified as described. Light petroleum refers to the fraction boiling between 40 and 60 °C, and was distilled through a 36 cm Vigreux column before use. Ether refers to diethyl ether; this, together with benzene and toluene, was dried where necessary by storage over sodium wire for several days. Tetrahydrofuran (THF) was distilled from potassium benzophenone ketyl under nitrogen prior to use. Dichloromethane and tetrachloromethane were dried where necessary by distillation from phosphorus pentaoxide. Dimethyl sulfoxide (DMSO) and dimethylformamide (DMF) were stirred for 15 h over barium oxide, decanted, and distilled under reduced pressure before storage over activated 4Å molecular sieves, under nitrogen. Pyridine, triethylamine, diisopropylamine, and *N*-isopropylcyclohexylamine were each distilled from, and stored over, potassium hydroxide pellets. Acetonitrile for photolyses was purified as follows: The reagent-grade solvent was dried by being stirred for 15 h over finely ground calcium hydride, and was then distilled. Phosphorus pentaoxide (5 g dm^{-3}) was added, and the mixture was stirred for a further 15 h before being redistilled through a 30 cm glass-packed column. Tryptophan in all cases refers to natural (*S*)-(−)-tryptophan, which was purchased from the Aldrich Chemical Company and used without further purification.

Photolyses were performed in a Rayonet type RS preparative photochemical reactor. Eight RUL 2537 Å lamps were used, giving a total output of 120 W predominantly (>99%) at 254 nm. Solutions of the substrates were placed in a quartz vessel, and degassed by passage of a steady stream of dry nitrogen through the solution for at least 30 min prior to, and during, irradiation. The pH of mixtures was monitored using indicator paper.

Analytical TLC was carried out on Merck Kieselgel 60 GF254 aluminium-backed plates. Visualisation was achieved by using UV light at 254 and 360 nm, iodine, and, in the case of indoles, by lightly spraying the plate with Ehrlich's reagent followed by gentle heating to produce a (usually) blue-purple colour. Ehrlich's reagent was prepared by addition of *p*-(dimethylamino)benzaldehyde (1 g) to a 25% solution of conc. hydrochloric acid in absolute ethanol (100 cm^3). Column chromatography refers to the flash method and was performed on Merck Kieselgel 60 H, under medium pressure provided by means of hand-bellows. The sample mixture was applied to the top of the column as a solution in a small amount of the column eluant, or by preadsorption onto silica.

Optical rotations ($[\alpha]_D$) were measured in the solvent specified by using a Perkin-Elmer 141 polarimeter. Units for $[\alpha]_D$ are in 10^{-1} deg cm^2 g^{-1}. IR spectra were recorded on either a Perkin-Elmer model 1710 or 883 Fourier transform IR spectrometer, the samples being analysed as thin films, Nujol mulls, or in solution, as indicated. UV–visible spectra were obtained by using a Philips PU 8740 scanning spectrophotometer, the samples being dissolved in spectroscopic-grade methanol. Fourier transform ^1H NMR spectra were recorded on either a Bruker WM 200 (200 MHz), a Bruker WM 250 (250 MHz), a JEOL GSX 270 (270 MHz), or a Bruker AM 500 (500 MHz) spectrometer. Chemical shifts are reported in parts per million downfield from $SiMe_4$ by reference to the residual protons of the respective solvents. Coupling constants (*J*) in Hertz are included where possible. ^{13}C Spectra were recorded on either the JEOL GSX 270 (67.9 MHz) or the Bruker WM 250 (62.9 MHz) instrument, and are referenced to the solvent. Electron-impact ionisation mass spectra were performed at Imperial College in the Organic Mass Spectrometry Laboratory, on an AEI MS 12 or a VG Micromass 7070 B mass spectrometer at an ionisation potential of 70 eV unless otherwise stated.

N-(*Chloroacetyl*)*tryptophan.*—Tryptophan (1.00 g, 4.90 mmol) was dissolved in 1.0 mol dm^{-3} sodium hydroxide (4.9 cm^3, 4.9 mmol) and the solution was cooled in an ice-bath. Chloroacetyl chloride (0.41 cm^3, 0.58 g, 5.1 mmol) was added dropwise to the shaken mixture during 15 min while the pH was maintained at 10–11 by the simultaneous addition of 5 mol dm^{-3} sodium hydroxide (1.1 cm^3, 5.5 mmol). The mixture was stirred at bath temperature for 10 min, then was transferred to a separatory funnel, where it was covered by a layer of ethyl acetate and acidified to pH 2 with 6 mol dm^{-3} hydrochloric acid. The aqueous layer was extracted twice more and the pooled organic extracts were dried over magnesium sulfate. Evaporation left an oil which solidified to a brown mass, recrystallisation of which from water gave tan leaflets of the title compound (1.11 g, 81%), m.p. 158–159 °C (lit.,[17] 159 °C); $[\alpha]_D$ +29.5 (*c* 0.80 in EtOH) [lit.,[18] +32.9 (*c* 5.58 in EtOH)];

Table 1 Crystal data and data-collection parameters

Compound	13	15	21	22	35
Formula	$C_{13}H_{14}N_2O_2$	$C_{14}H_{14}N_2O_3$	$C_{15}H_{16}N_2O_4$	$C_{14}H_{15}N_3O_4$	$C_{12}H_{10}N_2O_2$
M_w	230.3	258.3	288.3	289.3	214.2
Crystal system	Orthorhomic	Orthorhombic	Monoclinic	Orthorhombic	Triclinic
Crystal dimensions/mm	0.12 × 0.23 × 0.27	0.27 × 0.33 × 0.47	0.15 × 0.27 × 0.67	0.17 × 0.23 × 0.33	0.10 × 0.17 × 0.67
a/Å	8.549(2)	6.297(2)	9.002(2)	8.258(1)	8.605(2)
b/Å	10.456(2)	10.931(3)	7.510(2)	9.326(1)	9.898(2)
c/Å	12.230(3)	17.908(5)	10.710(3)	14.302(1)	12.878(2)
α/°	90	90	90	90	89.12(2)
β/°	90	90	113.58(2)	90	82.88(1)
γ/°	90	90	90	90	68.59(1)
V/Å^3	1093	1233	664	3599	1013
Z	4	4	2	8	4
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1$	$P22_12$	P-1
D_c/g cm^{-3}	1.40	1.39	1.44	1.18[a]	1.40
F(000)	488	544	306	1344	448
μ(Cu-Kα)	7	8	8	7	8
θ Range/°	0–58	0–58	0–58	0–58	0–58
No unique reflections	881	990	978	2757	2726
No. Observed reflections	850	970	964	2229	2456
No. variables	167	184	205	298	306
R	0.036	0.030	0.028	0.204	0.036
R_w[b]	0.045	0.037	0.031	0.206	0.040
g	0.000 77	0.000 33	0.000 46	0.001 00	0.000 29
Extinction parameter, x	0.016(3)	0.013(2)	0.041(4)		0.013(2)

[a] Compound **22** consisted of two independent molecules in the asymmetric unit, of which one was ordered, and one disordered, plus one molecule of acetone. This is taken into account in the density; the molecular weight given refers to one molecule of compound **22**. [b] $w^{-1} = \sigma(F) + g^2F^2$.

Table 2 Atom co-ordinates (× 10^4) for compound **13**

Atom	x	y	z
N(1)	1339(3)	1928(3)	7945(2)
C(2)	2529(4)	2792(3)	8092(3)
C(3)	3609(3)	2697(3)	7269(3)
C(3a)	3023(3)	1716(3)	6550(2)
C(4)	3550(3)	1231(3)	5546(3)
C(5)	2709(4)	267(3)	5061(3)
C(6)	1316(4)	−219(3)	5564(3)
C(7)	798(4)	245(3)	6530(3)
C(7a)	1641(3)	1245(3)	7000(3)
C(8)	5081(3)	3431(3)	7158(3)
C(9)	6612(4)	2670(3)	7318(2)
N(10)	6964(3)	1626(3)	6545(2)
C(11)	6455(4)	1219(3)	5561(3)
O(11)	7194(3)	311(2)	5137(2)
C(12)	5070(3)	1751(3)	5025(2)
C(13)	6652(4)	2053(3)	8440(3)
O(13)	8162(3)	1469(3)	8604(2)

Table 3 Atom co-ordinates (× 10^4) for compound **15**

Atom	x	y	z
N(1)	3 441(4)	1 509(2)	9 440(1)
C(2)	2 182(4)	558(2)	9 187(1)
C(3)	456(4)	1 016(2)	8 808(1)
C(3a)	615(4)	2 328(2)	8 846(1)
C(4)	−640(5)	3 290(2)	8 590(1)
C(5)	−9(5)	4 483(3)	8 733(1)
C(6)	1 880(5)	4 723(2)	9 112(2)
C(7)	3 158(5)	3 794(2)	9 372(2)
C(7a)	2 517(5)	2 606(2)	9 243(1)
C(8)	−1 275(4)	314(2)	8 430(1)
C(9)	−899(4)	−1 058(2)	8 422(1)
N(10)	−756(3)	−1 602(2)	9 170(1)
C(11)	896(4)	−1 477(2)	9 636(1)
O(11)	847(3)	−1 939(2)	10 264(1)
C(12)	2 776(4)	−745(2)	9 369(1)
C(13)	−2 709(4)	−1 706(2)	8 016(1)
O(13)	−4 248(4)	−1 213(2)	7 760(1)
O(14)	−2 392(3)	−2 908(2)	7 991(1)
C(15)	−4 120(6)	−3 631(2)	7 684(2)

δ_H(250 MHz; [$^2H_6$]acetone) 3.29 (1 H, dd, J 6.5 and 14.5, ArCH_2), 3.39 (1 H, dd, J 5.3 and 14.5, ArCH_2), 4.11 (2 H, s, COCH_2Cl), 4.80 (1 H, m, CHNHCO), 7.00 (1 H, t, J 7.4, 5-H), 7.08 (1 H, t, J 7.6, 6-H), 7.21 (1 H, s, 2-H), 7.36 (1 H, d, J 8.4, 7-H), 7.51 (1 H, br s, CHNHCO), 7.59 (1 H, d, J 7.6, 4-H) and 10.14 (1 H, br s, 1-H).

Irradiation of N-(*Chloroacetyl*)*tryptophan*.—A solution of *N*-chloroacetyltryptophan (245 g, 0.87 mmol) in water (100 cm^3) was irradiated for 45 min. The resulting cloudy yellow solution was extracted with ethyl acetate and the extracts were evaporated to give a brown resin. The crude products of twelve such trials of this reaction were combined together (total of 2.93 g having thus been irradiated), dissolved in methanol, and treated with excess of ethereal diazomethane. The solvent was stripped off and the tarry residue was dissolved in the minimum volume of methanol. On storage, a solid precipitated and was collected on a filter and washed with a small amount of methanol. This chromatographically homogeneous, sparingly soluble tan powder was identified as methyl 1,3,4,5,6,7-hexahydro-6-oxopyrrolo[4,3,2-*fg*][3]benzazocine-4-carboxylate **12** (644 mg, 24%), a small portion of which was recrystallised, m.p. 232–234 °C (from MeOH) (lit.,[11] 230–232 °C); $[\alpha]_D$ −107 (*c* 0.35 in EtOH) [lit.,[11] −55 ± 3 (*c* 0.35 in EtOH)]; ν_{max}(CHCl$_3$)/cm^{-1} 3476 (indole NH), 3384 (amide NH), 3004, 2956, 1744 (ester C=O), 1665 (amide C=O), 1466, 1437, 1341, 1283, 1160, 1088, 1003, 772 and 727; λ_{max}(MeOH)/nm 202 (log ε 4.36), 223 (4.34) and 282 (3.76); δ_H(250 MHz; [$^2H_6$]acetone) 3.60 (2 H, d, J 9.1, 3-H$_2$), 3.70 (1 H, d, J 12.9, 7-H), 3.78 (3 H, s, CO$_2$Me), 4.15 (1 H, d, J 12.1, 7-H), 4.48 (1 H, m, 4-H), 6.42 (1 H, br s, 5-H), 6.84 (1 H, d, J 7.2, 8-H), 6.99 (1 H, t, J 7.6, 9-H), 7.22 (1 H, s, 2-H), 7.26 (1 H), d, J 8.3, 10-H) and 10.19 (1 H, br s, 1-H); δ_C(62.9 MHz off-resonance decoupled; [$^2H_6$]DMSO) 28.4 (t, C-3), 41.4 (t, C-7), 52.0 (q, CO$_2$*Me*), 56.3 (d, C-4), 109.7 (s, C-2a), 110.2 (d, C-10), 119.5 (d, C-8), 121.0 (d, C-9), 123.6 (d, C-2), 125.7 (s, C-7a), 127.7 (s, C-10b), 136.1 (s, C-10a), 172.6 (s), and 172.9 (s); m/z 258

Table 4 Atom co-ordinates ($\times 10^4$) for compound **21**

Atom	*x*	*y*	*z*
N(1)	−1883(2)	2016(4)	9001(2)
C(2)	−748(3)	902(4)	8869(2)
C(2a)	55(2)	1729(4)	8189(2)
C(3)	1287(2)	940(4)	7739(2)
C(4)	3057(2)	1576(3)	8539(2)
N(5)	3310(2)	3429(3)	8957(2)
C(6)	2690(2)	4994(3)	8325(2)
O(6)	3210(2)	6416(3)	8892(2)
C(7)	1211(2)	4970(3)	6923(2)
O(7)	1206(2)	6502(3)	6163(2)
C(7a)	−270(2)	5005(4)	7273(2)
C(8)	−1181(2)	6520(4)	7133(2)
C(9)	−2456(3)	6570(4)	7584(2)
C(10)	−2794(3)	5149(4)	8210(2)
C(10a)	−1854(3)	3625(4)	8392(2)
C(10b)	−616(2)	3503(3)	7887(2)
C(11)	4062(2)	976(3)	7775(2)
O(11)	4854(2)	−375(3)	8028(2)
O(12)	3965(2)	2089(3)	6784(2)
C(12)	4817(3)	1596(5)	5953(3)
C(13)	2464(3)	6481(4)	5678(3)

Table 5 Atomic co-ordinates ($\times 10^4$) for compound **22**

Atom	*x*	*y*	*z*
N(1)	−2694(21)	1786(10)	213(9)
C(2)	−1905(15)	1223(11)	446(10)
C(2a)	−446(14)	1369(8)	291(9)
C(2b)	−390(12)	2054(7)	−55(8)
C(3)	791(16)	873(9)	429(7)
C(4)	1824(15)	1180(6)	925(7)
N(5)	2129(16)	1971(6)	922(6)
C(6)	2595(17)	2408(9)	493(5)
O(6)	3101(18)	3006(7)	605(7)
C(7)	2230(12)	2244(9)	−220(6)
N(7)	3233(20)	2585(9)	−631(7)
O(7)	4616(16)	2230(9)	−543(7)
C(7a)	723(12)	2471(8)	−307(8)
C(8)	386(18)	3110(9)	−607(10)
C(9)	−1176(17)	3317(12)	−673(15)
C(10)	−2286(23)	2949(9)	−443(10)
C(10a)	−1900(14)	2306(9)	−96(9)
C(11)	3361(17)	802(12)	863(9)
O(11)	4452(17)	1054(9)	721(8)
O(12)	3202(17)	72(7)	982(9)
C(12)	4470(32)	−366(13)	983(18)
N(1′)	5282(28)	4686(13)	2250(18)
C(2′)	3902(23)	4933(16)	2312(18)
C(2′a)	3970(26)	5660(17)	2529(25)
C(2′b)	5530(26)	5787(11)	2494(15)
C(3′)	2825(40)	6110(17)	2837(16)
C(4′)	2435(32)	6771(13)	2434(16)
N(5′)	3401(14)	7244(9)	2056(8)
C(6′)	4713(14)	7451(9)	2158(7)
O(6′)	5413(16)	7787(7)	1770(6)
C(7′)	5617(18)	7148(8)	2732(7)
N(7′)	6739(18)	7652(9)	2928(8)
O(7′)	6081(17)	8307(8)	3203(7)
C(7′a)	6266(26)	6438(9)	2591(15)
C(8′)	7714(27)	6476(18)	2450(16)
C(9′)	8558(50)	5781(20)	2397(36)
C(10′)	7944(23)	5195(17)	2155(15)
C(10′a)	6417(23)	5166(12)	2280(11)
C(11′)	1337(50)	7245(26)	2834(24)
O(11′)	150(50)	6998(24)	2914(22)
O(12′)	2060(26)	7699(11)	3024(11)
C(12′)	2648(29)	8396(11)	2925(13)
O(2#a)	748(31)	7700(14)	3304(12)
C(2#a)	539(58)	8293(19)	3716(19)
C(20)	878(67)	8779(32)	1578(27)
C(21)	−678(56)	8863(24)	1674(22)
O(21)	−1804(39)	8922(17)	1376(15)
C(22)	−1059(41)	8523(20)	2158(18)

(M$^+$, 83%), 199 (8, M − CO_2Me), 183 (5), 171 (24), 170 (23), 154 (23), 144 (79), 143 (100, M − $CONHCHCO_2Me$), 115 (31, Ar$^{\cdot+}$) and 85 (17).

The black filtrate was found by TLC to be a mixture of the above product and a slightly less polar material. The two compounds could not be completely separated chromatographically, but crystals of the less polar product separated from enriched early fractions. This material was the alternative cyclisation product, *methyl* 1,2,3,4,5,6-*hexahydro*-4-*oxoazepino*[4,5-b]*indole*-2-*carboxylate* **15**, m.p. 238–240 °C (Found: C, 65.1; H, 5.5; N, 10.8. $C_{14}H_{14}N_2O_3$ requires C, 65.1; H, 5.5; N, 10.9%); $[\alpha]_D$ −32.5 (*c* 1.00 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3465 (indole NH), 3382 (amide NH), 3004, 1744 (ester C=O), 1671 (amide C=O), 1461, 1434, 1383, 1329, 1314, 1277, 1206, 1154, 1005 and 643; λ_{max}(MeOH)/nm 200 (log ε 4.35), 220 (4.51), 281 (3.86) and 289 (3.80); δ_H(250 MHz; [$^2H_6$]acetone) 3.01 (1 H, dd, *J* 11.0 and 16.0, 1-H), 3.35 (1 H, dt, *J* 2.5 and 16.0, 1-H), 3.54 (1 H, d, *J* 16.0, 5-H), 3.83 (3 H, s, CO_2Me), 4.26 (1 H, d, *J* 17.0, 5-H), 4.90 (1 H, m, 2-H), 6.68 (1 H, br s, 3-H), 7.00 (1 H, t, *J* 7.0, 9-H), 7.07 (1 H, t, *J* 7.0, 8-H), 7.31 (1 H, d, *J* 8.0, 7-H), 7.40 (1 H, d, *J* 7.5, 10-H) and 10.08 (1 H, br s, 6-H); *m/z* 258 (M$^+$, 53%), 199 (5, M − CO_2Me), 170 (100), 144 (34), 143 (59, M − $CONHCHCO_2Me$), 130 (9) and 115 (11, Ar$^{\cdot+}$).

1,3,4,5,6,7-*Hexahydro*-4-*hydroxymethyl*-6-*oxopyrrolo*[4,3,2-fg][3]*benzazocine* **13**.—To a suspension of ester **12** (500 mg, 1.94 mmol) in (3:1) ethanol–water (20 cm^3) was added a solution of sodium borohydride (366 mg, 9.68 mmol) in (3:1) ethanol–water (10 cm^3). Complete solution was effected within 30 min, after which TLC revealed no remaining starting material. The reaction mixture was acidified to pH 2 with dil. hydrochloric acid, saturated with sodium chloride, and extracted with ethyl acetate. The combined extracts were dried over sodium sulfate and evaporated, to give a yellow solid, which was triturated with a small amount of methanol. The remaining microcrystalline powder was the analytically pure *title compound* **13** (197 mg), and another crop (77 mg) of the alcohol **13** was isolated from the filtrate by chromatography (15% EtOH–CH_2Cl_2); total yield 274 mg (61%), m.p. 246–248 °C (Found: C, 67.7; H, 6.1; N, 12.1. $C_{13}H_{14}N_2O_2$ requires C, 67.8; H, 6.1; N, 12.2%); $[\alpha]_D$ −96.5 (*c* 0.0705 in MeOH); ν_{max}(KBr)/cm^{-1} 3366, 3283br, 2927, 2890, 2851, 1625 (C=O), 1464, 1432, 1341, 1324, 1272, 1146, 1111, 1059, 1040, 768, 703 and 614; λ_{max}(MeOH)/nm 201 (log ε 4.33), 224 (4.36, 283 (3.78) and 290infl; δ_H(250 MHz; [$^2H_6$]acetone) 3.25 (1 H, dd, *J* 9.2 and 15.5, 3-H), 3.39 (1 H, dd, *J* 5.3 and 15.5, 3-H), 3.64 (1 H, dd, *J* 6.3 and 10.8, C*H*HOH), 3.73 (1 H, dd, *J* 5.1 and 10.8, CH*H*OH), 3.84 (1 H, d, *J* 11.7, 7-H), 3.88 (1 H, m, 4-H), 4.01 (1 H, d, *J* 12.0, 7-H), 6.14 (1 H, br s, 5-H), 6.82 (1 H, d, *J* 7.0, 8-H), 6.97 (1 H, t, *J* 7.4, 9-H), 7.15 (1 H, s, 2-H), 7.25 (1 H, d, *J* 8.2, 10-H) and 10.14 (1 H, br s, 1-H); *m/z* 230 (M$^+$, 26%), 199 (4, M − CH_2OH), 171 (11, M − $NHCHCH_2OH$), 149 (10), 144 (37), 143 (38, M − $CONHCHCH_2OH$), 115 (13, Ar$^{\cdot+}$), 45 (60) and 31 (100, $CH_2OH^{\cdot+}$).

4-(tert-*Butyldiphenylsiloxymethyl*)-1,3,4,5,6,7-*hexahydro*-6-*oxopyrrolo*[4,3,2-fg][3]*benzazocine* **14**.—To a solution of alcohol **13** (764 mg, 3.32 mmol) and imidazole (497 mg, 7.30 mmol) in dry DMF (12 ml) was added *tert*-butylchlorodiphenylsilane (0.95 cm^3, 1.0 g, 3.65 mmol). After 15 h the precipitated solid was filtered off from the reaction mixture and was washed with a small amount of methanol. The filtrate was evaporated, and triturated with methanol, to give more product

Table 6 Atom co-ordinates (× 10^4) for compound **35**

Atom	*x*	*y*	*z*
N(1)	226(2)	1931(2)	537(1)
C(2)	1010(3)	1048(2)	1278(2)
C(3)	2580(2)	1079(2)	1327(1)
C(4)	3730(3)	106(2)	2038(2)
C(5)	5518(3)	39(2)	1907(2)
N(6)	5662(2)	1360(2)	2303(1)
C(7)	5603(2)	2484(2)	1731(1)
O(7)	5521(2)	3673(2)	2071(1)
C(8)	5628(2)	2364(2)	551(1)
O(8)	6932(2)	2241(2)	−3(1)
C(9)	4036(2)	2633(2)	132(1)
C(10)	3742(3)	3561(2)	−704(1)
C(11)	2244(3)	4001(2)	−1135(2)
C(12)	997(3)	3517(2)	−758(2)
C(13)	1272(2)	2576(2)	67(1)
C(14)	2767(2)	2095(2)	552(1)
N(1′)	−1817(2)	4026(2)	7080(1)
C(2′)	−1487(2)	5272(2)	7020(1)
C(3′)	82(2)	5039(2)	6520(1)
C(4′)	689(2)	6275(2)	6300(1)
C(5′)	2355(2)	5911(2)	5623(1)
N(6′)	3753(2)	5070(1)	6175(1)
C(7′)	4438(2)	3644(2)	6128(1)
O(7′)	5544(1)	2895(1)	6643(1)
C(8′)	3853(2)	2832(2)	5357(1)
O(8′)	4810(2)	2308(1)	4559(1)
C(9′)	2322(2)	2521(2)	5684(1)
C(10′)	2446(2)	1102(2)	5478(2)
C(11′)	1173(3)	599(2)	5833(2)
C(12′)	−285(3)	1501(2)	6394(2)
C(13′)	−454(2)	2926(2)	6588(1)
C(14′)	810(2)	3504(2)	6240(1)

for a total yield of 1.19 g (76%) of the analytically pure *title compound* **14** as a microcrystalline solid, m.p. 210 °C (Found: C, 74.1; H, 6.8; N, 5.9. $C_{29}H_{32}N_2O_2Si$ requires C, 74.3; H, 6.9; N, 6.0%); $[\alpha]_D$ −26.0 (*c* 0.500 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3478 (indole NH), 3382 (amide NH), 3000, 2959, 2930, 2859, 1650 (C=O), 1463, 1428, 1339, 1204, 1111 (CH_2OSi), 938, 824, 807, 695 and 614; λ_{max}(MeOH)/nm 201 (log ε 4.70), 218 (4.58) and 283 (3.77); δ_H(250 MHz; [$^2H_6$]acetone) 1.10 (9 H, s, $SiCMe_3$), 3.35 (1 H, dd, *J* 5.9 and 15.9, 3-H), 3.49 (1 H, dd, *J* 9.7 and 15.8, 3-H), 3.84 (1 H, 7-H), 3.85 (2 H, m, CH_2OSi), 3.91 (1 H, m, 4-H), 4.11 (1 H, d, *J* 12.8, 7-H), 6.30 (1 H, br s, 5-H), 6.83 (1 H, d, *J* 7.1, 8-H), 6.98 (1 H, t, *J* 7.8, 9-H), 7.14 (1 H, s, 2-H), 7.25 (1 H, d, *J* 8.2, 10-H), 7.45 (6 H, m, SiPh *m*- and *p*-H), 7.75 (4 H, m, SiPh *o*-H) and 10.13 (1 H, br s, 1-H); δ_C(62.9 MHz; [$^2H_6$]DMSO) 18.7 ($SiCMe_3$), 26.6 ($SiCMe_3$), 28.1 (C-3), 41.8 (C-7), 55.9 (C-4), 67.1 (CH_2OSi), 110.2 (C-2a), 111.0 (C-10), 119.5 (C-8), 120.9 (C-9), 123.5 (C-2), 125.7 (C-7a), 127.7 (SiPh C-*ipso*), 128.1 (C-10b), 129.7 (SiPh C-*m*), 132.7 (SiPh C-*p*), 135.0 (SiPh C-*o*), 136.3 (C-10a) and 172.7 (C-6); *m*/*z* 468 (M^+, 7%), 411 (100, M − CMe_3), 333 (23), 240 (17), 199 (29, M − CH_2OSiR_3), 183 (7), 171 (19, M − $NHCHCH_2OSiR_3$), 162 (11), 154 (6), 144 (50), 143 (20), 135 (12), 115 (12, $Ar^{\bullet+}$) and 77 (6).

N-(*Chloroacetyl*)*tryptophan Methyl Ester* **16**.—A solution of *N*-(chloroacetyl)tryptophan (1.00 g, 3.56 mmol) in methanol (10 cm^3) was treated with excess of diazomethane in ether. The solvent was evaporated off and the resulting light yellow oil was purified by dry flash chromatography (light petroleum → ether → 5% methanol–ether gradient) to give the *title compound* **16** (0.939 g, 89%) as a glass which crystallised on storage, m.p. 133–134 °C (from benzene) (Found: C, 57.1; H, 5.2; N, 9.5. $C_{14}H_{15}ClN_2O_3$ requires C, 57.1; H, 5.1; N, 9.5%); $[\alpha]_D$ +11.0 (*c* 1.00 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3476 (indole NH), 3405 (amide NH), 3046, 2998, 2954, 1742 (ester C=O), 1675 (amide C=O), 1528, 1457, 1439, 1356, 1260, 1181, 1092 and 805; λ_{max}(MeOH)/nm 219 (log ε 4.52), 280 (3.75), and 289infl; δ_H(250 MHz; [$^2H_6$]acetone) 3.25 (1 H, dd, *J* 6.8 and 14.5, ArC*H*H), 3.33 (1 H, dd, *J* 5.6 and 14.5, ArCH*H*), 3.65 (3 H, s, CO_2Me), 4.10 (2 H, s, $COCH_2Cl$), 4.77 (1 H, m, C*H*NHCO), 7.02 (1 H, t, *J* 7.3, 5-H), 7.09 (1 H, t, *J* 7.3, 6-H), 7.20 (1 H, s, 2-H), 7.37 (1 H, d, *J* 8.0, 7-H), 7.54 (1 H, d, *J* 7.5, 4-H), 7.61 (1 H, br s, CHN*H*CO) and 10.19 (1 H, br s, 1-H); *m*/*z* 294 (M^+, 7%), 201 (13, M − H_2NCOCH_2Cl), 170 (2), 130 (100, $ArCH_2^{\bullet+}$), 103 (4) and 77 (5).

Irradiation of N-(*chloroacetyl*)*tryptophan Methyl Ester* **16**.—A solution of *N*-(chloroacetyl)tryptophan methyl ester **16** (681 mg, 2.31 mmol) in acetonitrile (120 cm^3) was irradiated for 3.5 h. The solvent was evaporated off and the resulting dark brown resin was taken up in methanol and adsorbed onto the minimum amount of silica gel. This was applied to the top of a dry flash column through which increasingly polar eluents were passed, starting with light petroleum containing increasing proportions of ether and finishing with 22% methanol–ether. Those fractions enriched in the correct isomer were combined and evaporated and the residue was triturated with methanol, to give chromatographically homogeneous methyl 1,3,4,5,6,7-hexahydro-6-oxopyrrolo[4,3,2-*fg*][3]benzazocine-4-carboxylate **12** (205 mg, 34%).

N-(*Bromoacetyl*)*tryptophan Methyl Ester* **17**.—The procedure was identical with that for the *N*-(chloroacetyl)tryptophan **16**, substituting bromoacetyl chloride (0.44 cm^3, 0.85 g, 5.4 mmol) for chloroacetyl chloride. The product acid was dissolved in methanol and treated with excess of diazomethane in ether. Evaporation of the solvent gave a light brown solid, which was chromatographed (20% Et_2O–CH_2Cl_2) to give the *title compound* **17** (1.30 g, 78%) as crystals, m.p. 141–142 °C (Found: C, 49.6; H, 4.4; N, 8.2. $C_{14}H_{15}BrN_2O_3$ requires C, 49.6; H, 4.5; N, 8.3%); $[\alpha]_D$ +17.3 (*c* 2.00 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3478 (indole NH), 3400 (amide NH), 3011, 2956, 1744 (ester C=O), 1671 (amide C=O), 1523, 1458, 1441, 1421, 1360, 1093, 1012 and 988; λ_{max}(MeOH)/nm 218 (log ε 4.54) and 279 (3.76); δ_H(250 MHz; [$^2H_6$]acetone) 3.23 (1 H, dd, *J* 6.7 and 14.4, ArC*H*H), 3.31 (1 H, dd, *J* 5.6 and 14.4, ArCH*H*), 3.65 (3 H, s, CO_2Me), 3.92 (2 H, s, $COCH_2Br$), 4.76 (1 H, m, C*H*NHCO), 7.02 (1 H, t, *J* 7.2, 5-H), 7.09 (1 H, t, *J* 7.2, 6-H), 7.20 (1 H, s, 2-H), 7.37 (1 H, d, *J* 8.0, 7-H), 7.54 (1 H, d, *J* 7.8, 4-H), 7.67 (1 H, br s, CHN*H*CO) and 10.13 (1 H, br s, 1-H); *m*/*z* 338 (M^+, 2%), 201 (11, M − H_2NCOCH_2Br), 170 (3), 149 (3) and 130 (100, $ArCH_2^{\bullet+}$).

N-(*Iodoacetyl*)*tryptophan Methyl Ester* **18**.—*N*-(Bromoacetyl)tryptophan methyl ester **17** (400 mg, 1.18 mmol) and sodium iodide (884 mg, 5.90 mmol) were introduced into a 25-cm^3 round-bottomed flask with stirring bar. Stirring was initiated and acetone (4 cm^3) was added to the solid mixture all at once. After 10 min the slurry was evaporated to dryness and the solid residue was partitioned between dichloromethane and water. The organic layer was separated, washed twice with water, and dried over magnesium sulfate. Evaporation of the solvent, and seeding with a minute crystal of the starting material, gave the analytically pure *title compound* **18** (440 mg, 97%) in the form of a pale yellow crystalline powder, m.p. 115–116 °C (Found: C, 43.8; H, 3.9; N, 7.2. $C_{14}H_{15}IN_2O_3$ requires C, 43.5; H, 3.9; N, 7.3%); $[\alpha]_D$ +17.0 (*c* 2.00 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3478 (indole NH), 3412 (amide NH), 3010, 2955, 1742, (ester C=O), 1673 (amide C=O), 1516, 1458, 1442, 1422, 1360, 1181, 1134, 1093, 1011 and 988; λ_{max}(MeOH)/nm 218 (log ε 4.55) and 279 (3.80); δ_H(250 MHz; [$^2H_6$]acetone) 3.21 (1 H, dd, *J* 6.7 and 14.7, ArC*H*H), 3.28 (1 H, dd, *J* 5.6 and 14.7, ArHC*H*), 3.65 (3 H, s, CO_2Me), 3.80 (2 H, s, $COCH_2I$),

4.76 (1 H, m, C*H*NHCO), 7.03 (1 H, t, *J* 7.4, 5-H), 7.10 (1 H, t, *J* 7.5, 6-H), 7.21 (1 H, s, 2-H), 7.38 (1 H, d, *J* 7.8, 7-H), 7.55 (1 H, d, *J* 7.8, 4-H), 7.73 (1 H, br s, CHN*H*CO) and 10.15 (1 H, br s, 1-H); *m/z* 386 (M^+, 6%), 231 (2), 201 (18, M − H_2NCOCH_2I), 144 (7) and 130 (100, $ArCH_2^{\bullet+}$).

Quantitative Analysis and Rate Study of the Irradiation of N-*Chloroacetyl* (**16**)-, N-*Bromoacetyl* (**17**)-, *and* N-*Iodoacetyl* (**18**)-*tryptophan Methyl Ester*.—Solutions of *N*-chloroacetyl (**16**)-, *N*-bromoacetyl (**17**)-, and *N*-iodoacetyl (**18**)-tryptophan methyl ester in acetonitrile (2 mg per cm^3) were irradiated and analysed at intervals of t = 1, 5, 14, 25, 45, and, in the case of *N*-(iodoacetyl)tryptophan methyl ester **18**, 75 min. A quantitative analysis was performed by removal of an aliquot (1 cm^3) at each interval, evaporation to dryness, and redissolution of the analyte in the chromatography solvent (40% water–methanol) (20 cm^3). Of this, a portion (18 mm^3) was taken and injected onto an ODS microanalytical HPLC column and eluted with the above mentioned solvent at the rate of 1.0 cm^3 min^{-1}. Peaks registered at 265 nm were integrated by the clip-and-weigh method and the area was expressed in terms of concentration by co-analysis of standard solutions of the product and starting materials to obtain conversion factors. First-order rate constants (k_1) were calculated by substituting the data into eqn. (1) for the idealised equation **A** ⟶ **B** (below); the results of this investigation were discussed in the text.

$$k_{t_2} = \frac{1}{t_2 - t_1} \ln \frac{[\mathbf{A}]_{t_1}}{[\mathbf{A}]_{t_2}} \qquad (1)$$

N-(*Dichloroacetyl*)*tryptophan Methyl Ester* **19**.—A two-phase system of tryptophan methyl ester (3.50 g, 16.0 mmol) in dichloromethane (30 cm^3) and sodium hydrogen carbonate (2.70 g, 32.1 mmol) in water (30 cm^3) was stirred vigorously at 0 °C while a solution of dichloroacetyl chloride (2.60 g, 17.6 mmol) in dichloromethane (10 cm^3) was added dropwise during 15 min. The reaction mixture was kept for an additional 1 h at 0 °C, then poured into water and extracted with dichloromethane. The combined organic layer was dried over sodium sulfate and evaporated, to give the *title compound* **19** (5.18 g, 98%) as an off-white solid, m.p. 115–122 °C. This material was chromatographically homogeneous and sufficiently pure for use, but recrystallisation of a small portion from ethyl acetate–light petroleum gave crystals, m.p. 124.5–125 °C (Found: C, 51.1; H, 4.2; N, 8.5. $C_{14}H_{14}Cl_2N_2O_3$ requires C, 51.1; H, 4.3; N, 8.5%); $[\alpha]_D$ +23.9 (*c* 1.625 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3476 (indole NH), 3403 (amide NH), 3006, 1742 (ester C=O), 1692 (amide C=O), 1522, 1457, 1441, 1364, 1250, 1183, 1092, 812, 776, 743 and 720; λ_{max}(MeOH)/nm 219 (log ε 4.55), 280 (3.76) and 289infl; δ_H(250 MHz; [$^2H_6$]acetone) 3.29 (1 H, dd, *J* 6.6 and 14.9, ArC*H*H), 3.37 (1 H, dd, *J* 5.6 and 14.9, ArCH*H*), 3.68 (3 H, s, CO_2Me), 4.78 (1 H, m, C*H*NHCO), 6.43 (1 H, s, $COCHCl_2$), 7.02 (1 H, t, *J* 7.3, 5-H), 7.09 (1 H, t, *J* 7.6, 6-H), 7.19 (1 H, s, 2-H), 7.37 (1 H, d, *J* 8.1, 7-H), 7.53 (1 H, d, *J* 7.8, 4-H), 7.93 (1 H, br s, CHN*H*CO) and 10.16 (1 H, br s, 1-H); *m/z* 328 (M^+, 4%), 269 (1, M − CO_2Me), 245 (1, M − $CHCl_2$), 201 (6, M − $H_2NCOCHCl_2$), 170 (2), 158 (1), 130 (100, $ArCH_2^{\bullet+}$), 103 (3) and 77 (4).

1,3,4,5,6,7-*Hexahydro*-7-*hydroxy*-6-*oxopyrrolo*[4,3,2-fg][3]-*benzazocine*-4-*carboxylate* **20**.—A solution of *N*-(dichloroacetyl)tryptophan methyl ester **19** (256 mg, 0.778 mmol) in acetonitrile (100 cm^3) was irradiated for 1 h. The solvent was evaporated off and the residue was chromatographed (30% EtOAc–Et_2O) to give the *title compound* **20** (123 mg, 58%) as a light brown, amorphous powder (Found: M^+, 274.0958. $C_{14}H_{14}N_2O_4$ requires M, 274.0954; $[\alpha]_D$ −96.4 (*c* 0.44 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3477 (indole NH), 3386 (amide NH), 3027, 1746 (ester C=O), 1671 (amide C=O), 1461, 1438, 1419, 1381, 1323, 1282, 1173, 1112, 1013, 986, 918, 854 and 834; λ_{max}(MeOH)/nm 204 (log ε 4.39), 222 (4.34) and 285 (3.78); δ_H(250 MHz; [$^2H_6$]acetone) 3.60 (2 H, m, 3-H_2), 3.78 (3 H, s, CO_2Me), 4.31 (1 H, m, 4-H), 4.45 (1 H, br d, OH), 6.15 (1 H, br d, 7-H), 7.06 (1 H, t, *J* 7.4, 9-H), 7.23 (1 H, d, *J* 7.3, 8-H), 7.26 (1 H, s, 2-H), 7.27 (1 H, d, *J* 8.1, 10-H) and 10.20 (1 H, br s, 1-H); *m/z* 274 (M^+, 100%), 185 (32), 170 (56), 159 (54), 158 (68), 130 (77), 115 (24, $Ar^{\bullet+}$), 77 (22), 58 (24) and 43 (77).

Methyl 1,3,4,5,6,7-*Hexahydro*-7-*methoxy*-6-*oxopyrrolo*[4,3,2-fg][3]*benzazocine*-4-*carboxylate* **21**.—A solution of *N*-(dichloroacetyl)tryptophan methyl ester **19** (258 mg, 0.784 mmol) in acetonitrile (100 cm^3) was irradiated for 1 h. The solvent was evaporated off and the residue was chromatographed (8% MeOH–CH_2Cl_2) to give the *title compound* **21** (143 mg, 63%) as a yellow resin. Slow evaporation of a solution of compound **21** in acetone caused light yellow crystals to separate, m.p. 224–229 °C after evolving gas at 190–191 °C (Found: M^+, 288.1109. $C_{15}H_{16}N_2O_4$ requires M, 288.1110); $[\alpha]_D$ −93.7 (*c* 0.413 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3478 (indole NH), 3388 (amide NH), 3008, 2956, 2930, 2857, 1743 (ester C=O), 1677 (amide C=O), 1460, 1438, 1419, 1347, 1284, 1171, 1125, 1086, 1015, 966, 838 and 816; λ_{max}(MeOH)/nm 202 (log ε 4.39), 225 (4.28) and 286 (3.72); δ_H(250 MHz; [$^2H_6$]acetone) 3.56 (3 H, s, 7-OMe), 3.61 (2 H, m, 3-H_2), 3.81 (3 H, s, CO_2Me), 4.30 (1 H, m, 4-H), 5.86 (1 H, s, 7-H), 6.71 (1 H, br d, 5-H), 7.03 (1 H, t, *J* 7.5, 9-H), 7.18 (1 H, d, *J* 7.2, 8-H), 7.23 (1 H, s, 2-H), 7.25 (1 H, 10-H) and 10.23 (1 H, br s, 1-H); δ_C(62.9 MHz modulated spin echo experiment; [$^2H_6$]DMSO) 28.7 (C-3), 52.1 (CO_2Me), 56.0 (C-4), 56.6 (7-OMe), 78.1 (C-7), 109.2 (C-2a), 110.5 (C-10), 113.9 (C-8), 121.1 (C-9), 123.7 (C-2), 124.0 (C-10b), 130.1 (C-7a), 136.1 (C-10a), 172.9, and 173.6; *m/z* 288 (M^+, 100%), 273 (34, M − Me), 245 (6), 229 (20, M − CO_2Me), 213 (20), 198 (14, M − OMe − CO_2Me), 174 (52), 170 (40), 169 (46), 158 (50), 154 (46), 144 (22), 130 (46), 115 (30, $Ar^{\bullet+}$) and 47 (52).

Methyl 1,3,4,5,6,7-*Hexahydro*-7-*hydroxyamino*-6-*oxopyrrolo*-[4,3,2-fg][3]*benzazocine*-4-*carboxylate* **22**.—A solution of *N*-(dichloroacetyl)tryptophan methyl ester **19** (303 mg, 0.920 mmol) in acetonitrile (100 cm^3) was irradiated for 70 min. The resulting rust-coloured solution was evaporated to a volume of ~10 cm^3, and a solution of hydroxylamine, which was prepared from hydroxylamine hydrochloride (500 mg, 7.2 mmol) and potassium hydroxide (400 mg, 7.1 mmol) in water (2 cm^3), was added to the shaken mixture. The reaction mixture could be decanted from the precipitated salts, which were then thoroughly washed with acetonitrile and discarded. The solvent was evaporated off and the residue was purified by chromatography (9% MeOH–CH_2Cl_2) to give the *title compound* **22** (135 mg, 51%) as a brown powder. Slow evaporation of solutions of compound **22** in acetone gave cubes, m.p. 130 °C with vigorous gas evolution (Found: M^+, 289.1062. $C_{14}H_{15}N_3O_4$ requires M, 289.1063); $[\alpha]_D$ −41.2 (*c* 0.600 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3478 (indole NH), 3264, 1742 (ester C=O), 1670 (amide C=O), 1603, 1559, 1541, 1522, 1508, 1459, 1436, 1420, 1340, 1285, 1173 and 992; δ_H(250 MHz; [$^2H_6$]acetone) 3.45–3.70 (2 H, br m, 3-H_2), 3.74 (3 H, s, CO_2Me), 4.26 (1 H, m, 4-H), 5.57 (1 H, br s, 7-H), 6.86 (1 H, d, *J* 7.1, 8-H), 7.01 (1 H, t, *J* 7.8, 9-H), 7.24 (1 H, s, 2-H), 7.26 (1 H, 10-H) and 10.18 (1 H, br s, 1-H); δ_C(62.9 MHz modulated spin echo experiment; [$^2H_6$]DMSO) 27.8 (C-3), 51.6 (CO_2Me), 55.9 (C-4), 64.0 (C-7), 109.0 (C-2a), 110 (C-10), 114.0 (C-8), 120.8 (C-9), 123.3 (C-2), 124.4 (C-10b), 128.9 (C-7a), 135.7 (C-10a), 172.1 and 174.4; *m/z* 289 (M^+, 2%), 273 (12), 272 (10), 271 (23, M − H_2O), 258 (4 − OMe), 241 (4), 226 (11), 212 (8), 195 (5), 184 (10), 169 (31), 156 (42), 155 (100), 142 (19), 130 (26), 115 (9, $Ar^{\bullet+}$), 44 (86) and 31 (42).

Irradiation of N-(*Dichloroacetyl*)*tryptophan Methyl Ester* **19** *in Aqueous Solution.*—A solution of *N*-(dichloroacetyl)tryptophan methyl ester **19** (200 mg, 0.608 mmol) in (80:20) acetonitrile–water (100 cm^3) was irradiated for 1 h. Most of the acetonitrile was stripped off under reduced pressure and the resulting cloudy solution was diluted with water (100 cm^3) and extracted with dichloromethane. The extracts were dried over sodium sulfate and evaporated, and chromatography (6% MeOH–CH_2Cl_2) of the residue gave alcohol **20** (36 mg, 21%) and 1,3,4,5,6,7-*hexahydro*-6,12-*dioxo*-7,4-(*epoxymethano*)*pyrrolo*[4,3,2-fg][3]*benzazocine* **23** (27 mg, 18%), as a pale yellow solid, m.p. >300 °C (Found: C, 64.4; H, 4.2; N, 11.4. $C_{13}H_{10}N_2O_3$ requires C, 64.5; H, 4.2; N, 11.6%); $[\alpha]_D$ +252 (*c* 0.190 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3475 (indole NH), 3398 (amide NH), 3027, 1752 (ester C=O), 1701 (amide C=O), 1437, 1399, 1366, 1322, 1192, 1164, 1111, 1032, 994 and 926; λ_{max}(MeOH)/nm 201 (log ε 4.28), 224 (4.30) and 294 (3.75); δ_H(250 MHz; [$^2H_6$]acetone) 3.71 (2 H, m, 3-H_2), 4.71 (1 H, m, 4-H), 5.68 (1 H, s, 7-H), 7.10 (1 H, t, *J* 7.5, 9-H), 7.16 (1 H, dd, *J* 1.5 and 7.1, 8-H), 7.36 (1 H, s, 2-H), 7.52 (1 H, dd, *J* 1.5 and 7.8, 10-H), 7.88 (1 H, br s, 5-H) and 10.72 (1 H, br s, 1-H); *m/z* 242 (M^+, 100%), 198 (6, M − CO_2), 170 (43, M − CO_2 − CO), 158 (32), 154 (13), 143 (12), 130 (28) and 115 (24, $Ar^{\bullet+}$).

N-(*Dichloroacetyl*)*tryptophanol* **24**.—A solution of *N*-(dichloroacetyl)tryptophan methyl ester **19** (200 mg, 0.61 mmol) in ethanol (3 cm^3) was added dropwise to a solution of sodium borohydride (115 mg, 3.0 mmol) in water (2 cm^3) at 0 °C. After 24 h the reaction mixture was warmed to room temperature and methanol (1 cm^3) was added to give a homogeneous solution, which was stored for 2 h before being evaporated to minimum volume. Water (50 cm^3) was added and the solution was saturated with salt and extracted with ethyl acetate. The extracts were pooled and dried over magnesium sulfate, and evaporation of the solvent gave an off-white solid (172 mg), which was purified by chromatography (0.5% MeOH–Et_2O) to yield the *title compound* **24** (130 mg, 71%) in the form of a white crystalline mass, m.p. 118 °C (Found: C, 52.0; H, 4.7; N, 9.3. $C_{13}H_{14}Cl_2N_2O_2$ requires C, 51.8; H, 4.7; N, 9.3%); $[\alpha]_D$ −19.8 (*c* 2.00 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3478 (indole NH), 3409 (amide NH), 3031, 1688 (C=O), 1522, 1457, 1337 and 1090; λ_{max}(MeOH)/nm 219 (log ε 4.54) and 279 (3.81); δ_H(250 MHz; [$^2H_6$]acetone) 3.01 (1 H, dd, *J* 6.6 and 14.6, ArC*H*H), 3.09 (1 H, dd, *J* 7.4 and 14.8, ArCH*H*), 3.62 (2 H, m, CH_2OH), 4.18 (1 H, m, C*H*NHCO), 6.36 (1 H, s, $COCHCl_2$), 7.01 (1 H, t, *J* 7.4, 5-H), 7.08 (1 H, t, *J* 7.5, 6-H), 7.18 (1 H, s, 2-H), 7.36 (1 H, d, *J* 8.0, 7-H), 7.64 (1 H, br s, CHN*H*CO), 7.70 (1 H, d, *J* 7.6, 4-H) and 10.07 (1 H, br s, 1-H); *m/z* 300 (M^+, 6%), 173 (24, M − $H_2NCOCHCl_2$), 149 (5), 130 (100, $ArCH_2^{\bullet+}$), 117 (7), 103 (5) and 77 (7).

Irradiation of N-(*Dichloroacetyl*)*tryptophanol* **24** *and Treatment with Sodium Azide.*—A solution of *N*-(dichloroacetyl)-tryptophanol **24** (301 mg, 1.00 mmol) in acetonitrile (100 cm^3) was irradiated for 30 min. The resulting opaque, dark green reaction mixture was evaporated to ~20 cm^3 and saturated aq. sodium azide (1.0 cm^3) was added to the vigorously stirred mixture. The mixture was evaporated to dryness and the residue was chromatographed (8% MeOH–CH_2Cl_2). The first of two compounds to elute was 1,3,4,5,6,7-*hexahydro*-6-*oxo*-7,4-(*epoxymethano*)*pyrrolo*[4,3,2-fg][3]*benzazocine* **25** (28 mg, 12%), which precipitated from early fractions as highly insoluble, hexagonal crystals, m.p. >300 °C (Found: M^+, 228.0896. $C_{13}H_{12}N_2O_2$ requires M, 228.0899); $[\alpha]_D$ +110.0 (*c* 0.100 in MeOH); ν_{max}(KBr)/cm^{-1} 3403, 3229, 3114, 2929, 2878, 1677 (C=O), 1640, 1439, 1414, 1356, 1339, 1322, 1133, 1117, 940, 793, 758, 731 and 625; λ_{max}(MeOH)/nm 202 (log ε 4.32), 227 (4.29) and 291 (3.81); δ_H(250 MHz; [$^2H_6$]acetone) 3.28 (1 H, d, *J* 16.8, 3-H), 3.55 (1 H, dd, *J* 7.7 and 17.0, 3-H), 4.07 (3 H, m, 4-H and 12-H_2), 5.05 (1 H, s, 7-H), 6.92 (1 H, d, *J* 7.2, 8-H), 6.97 (1 H, t, *J* 7.4, 9-H), 7.18 (1 H, s, 2-H) and 7.33 (1 H, dd, *J* 1.7 and 7.4, 10-H); *m/z* 228 (M^+, 100%), 199 (3), 185 (8), 170 (29), 158 (33), 149 (6), 143 (9), 130 (40), 115 (15, $Ar^{\bullet+}$), 103 (9), 77 (16) and 44 (33).

Continued chromatography gave 7-*azido*-1,3,4,5,6,7-*hexahydro*-4-*hydroxymethyl*-6-*oxopyrrolo*[4,3,2-fg][3]*benzazocine* **26** (25 mg, 9%), m.p. 215–218 °C with evolution of gas (Found: M^+, 271.1071. $C_{13}H_{13}N_5O_2$ requires M, 271.1069); $[\alpha]_D$ −137.2 (*c* 0.634 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3478 (indole NH), 2113 (N_3), 1668 (C=O), 1524, 1461, 1435, 1343, 1289 and 919; δ_H(270 MHz; [$^2H_6$]acetone) 3.20 (1 H, br d, 3-H), 3.66 (1 H, br m, 3-H), 3.82 (2 H, br s, CH_2OH), 4.49 (1 H, t, 4-H), 6.43 (1 H, br s, 7-H), 6.58 (1 H, br s, 5-H), 7.07 (1 H, t, *J* 7.6, 9-H), 7.11 (1 H, d, *J* 7.1, 8-H), 7.20 (1 H, br d, 2-H), 7.30 (1 H, d, *J* 7.6, 10-H) and 10.13 (1 H, br s, 1-H); *m/z* 271 (M^+, 31%), 243 (100, M − N_2), 230 (29), 228 (85), 225 (13), 200 (12), 197 (14), 185 (26), 170 (44), 156 (31), 155 (31), 143 (42), 130 (26), 115 (23, $Ar^{\bullet+}$), 102 (7), 77 (14) and 43 (22).

α-(tert-*Butyldimethylsiloxymethyl*)-N-(*dichloroacetyl*)*tryptophamine* **27**.—A mixture of *N*-(dichloroacetyl)tryptophanol **24** (200 mg, 0.66 mmol), TBDMSCl (100 mg, 0.73 mmol), and imidazole (100 mg, 1.5 mmol) in DMF (2 cm^3) was stirred for 18 h at room temperature. Most of the solvent was removed under reduced pressure and the residue was chromatographed (ether) to yield the *title compound* **27** (233 mg, 84%) as a clear resin (Found: C, 54.7; H, 6.8; N, 6.5. $C_{19}H_{28}Cl_2N_2O_2Si$ requires C, 54.9; H, 6.8; N, 6.7%); $[\alpha]_D$ −27.5 (*c* 0.880 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3478 (indole NH), 3415 (amide NH), 3031, 2954, 2929, 2857, 1688 (C=O), 1518, 1457, 1254, 1115 (CH_2OSi), 1090, 836, 812 and 712; λ_{max}(MeOH)/nm 219 (log ε 4.54) and 279 (3.76); δ_H(250 MHz; [$^2H_6$]acetone) 0.07 (3 H, s, SiMe), 0.08 (3 H, s, SiMe), 0.93 (9 H, s, $SiCMe_3$), 2.99 (1 H,dd, *J* 6.8 and 14.6, ArC*H*H), 3.12 (1 H, dd, *J* 7.1 and 14.6, ArCH*H*), 3.71 (2 H, d, *J* 4.9, CH_2OSi), 4.22 (1 H, m, C*H*NHCO), 6.33 (1 H, s, $COCHCl_2$), 7.01 (1 H, t, *J* 7.4, 5-H), 7.09 (1 H, t, *J* 7.5, 6-H), 7.18 (1 H, s, 2-H), 7.37 (1 H, d, *J* 8.1, 7-H), 7.58 (1 H, br s, CHN*H*CO), 7.67 (1 H, d, *J* 7.8, 4-H) and 10.10 (1 H, br s, 1-H); *m/z* 414 (M^+, 8%), 380 (3), 357 (30, M − CMe_3), 323 (9), 287 (28, M − $H_2NCOCHCl_2$), 230 (27), 186 (5), 184 (7), 156 (21), 130 (100, $ArCH_2^{\bullet+}$) and 116 (7, $Ar^{\bullet+}$).

7-*Azido*-4-(tert-*butyldimethylsiloxymethyl*)-1,3,4,5,6,7-*hexahydro*-6-*oxopyrrolo*[4,3,2-fg][3]*benzazocine* **28**.—A solution of the *N*-(dichloroacetyl)tryptophanol *tert*-butyldimethylsilyl derivative **27** (204 mg, 0.49 mmol) in acetonitrile (100 cm^3) was irradiated for 45 min. The solution was evaporated to ~20 cm^3 and a solution of sodium azide (96 mg, 1.5 mmol) in water (2 cm^3) was added to the shaken mixture. The reaction mixture was then diluted with dichloromethane (100 cm^3) and dried with sodium sulfate. The solvent was evaporated off and the residue was chromatographed (5% MeOH–CH_2Cl_2) to give the *title compound* **28** (68 mg, 36%) in the form of a light brown resin (Found: M − N_2, 357.1872. $C_{19}H_{27}N_3O_2Si$ requires *m/z*, 357.1873); $[\alpha]_D$ −121.7 (*c* 0.235 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3477 (indole NH), 3384 (amide NH), 3029, 3009, 2955, 2931, 2885, 2859, 2112 (N_3), 1668 (C=O), 1463, 1435, 1420, 1343, 1260, 1112, (CH_2OSi), 1015, 944 and 838; λ_{max}(MeOH)/nm 203 (log ε 4.38) and 289 (3.79); δ_H(250 MHz; [$^2H_6$]acetone) 0.18 (6 H, s, $SiMe_2$), 0.98 (9 H, s, $SiCMe_3$), 3.19 (1 H, br d, 3-H), 3.68 (2 H, br m, 3- and 4-H), 3.92 (2 H, br s, CH_2OSi), 6.29 (1 H, br s, 7-H), 6.70 (1 H, br s, 5-H), 7.08 (1 H, t, *J* 7.6, 9-H), 7.15 (1 H, d, *J* 7.1, 8-H), 7.21 (1 H, s, 2-H), 7.31 (1 H, d, *J* 7.7, 10-H) and 10.20 (1 H, br s, 1-H); *m/z* 385 (M^+, 0.2%), 359 (3), 357 (4, M − N_2), 344 (4), 328 (1, M − CMe_3), 300 (5, M − N_2 − CMe_3), 287 (3), 255

(2), 225 (2), 212 (1), 184 (3), 182 (4), 174 (2), 171 (3), 169 (3), 156 (6), 149 (2), 143 (4), 132 (5), 116 (4) and 75 (100).

Desilylation of Compound **28**.—A solution of silyloxy derivative **28** (60 mg, 0.16 mmol) in (3:1:1) acetic acid–THF–water (2 cm^3) was heated at 75 °C for 3.5 h. The reaction mixture was transferred to a separatory funnel containing 10% aq. sodium hydrogen carbonate (100 cm^3) and was extracted with dichloromethane. The extracts were dried over sodium sulfate, then evaporated, and the residue was chromatographed (7% MeOH–CH_2Cl_2) to yield a product indistinguishable (TLC, NMR) from azido alcohol **26** (6.4 mg, 15%).

N-(*Trichloroacetyl*)*tryptophan Methyl Ester* **29**.—A two-phase system of tryptophan methyl ester (300 mg, 1.4 mmol) in dichloromethane (5 cm^3) and sodium carbonate (318 mg, 3.0 mmol) in water (3 cm^3) was vigorously stirred at 0 °C while a solution of trichloroacetyl chloride (275 mg, 1.5 mmol) in dichloromethane (5 cm^3) was added dropwise. The reaction mixture was kept for an additional 1 h at 0 °C, during which the majority of the *title compound* **29** crystallised out of the reaction mixture. This product was collected on a filter and the filtrate was diluted with water and extracted with dichloromethane, to provide an additional crop of compound **29**, the whole of which was combined and recrystallised from methanol to give rod-shaped crystals (433 mg, 87%), m.p. 176–178 °C (Found: C, 46.3; H, 3.5; N, 7.7. $C_{14}H_{13}Cl_3N_2O_3$ requires C, 46.2; H, 3.6; N, 7.7%); $[\alpha]_D$ −22.0 (*c* 1.00 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3476 (indole NH), 3403 (amide NH), 3037, 3019, 2954, 1744 (ester C=O), 1711 (amide C=O), 1599, 1511, 1457, 1441, 1360, 1237, 1092, 1011 and 822 (CCl_3); λ_{max}(MeOH)/nm 217 (log ε 4.53) and 277 (3.76); δ_H(250 MHz; [$^2H_6$]acetone) 3.37 (1 H, dd, *J* 7.6 and 14.9, ArC*H*H), 3.46 (1 H, dd, *J* 5.2 and 14.9, ArCH*H*), 3.72 (3 H, s, CO_2Me), 4.76 (1 H, m, C*H*NHCO), 7.03 (1 H, t, *J* 7.3, 5-H), 7.10 (1 H, t, *J* 7.5, 6-H), 7.25 (1 H, s, 2-H), 7.38 (1 H, d, *J* 7.8, 7-H), 7.58 (1 H, d, *J* 7.8, 4-H), 8.18 (1 H, br s, CHN*H*CO) and 10.20 (1 H, br s, 1-H); *m/z* 362 (M^+, 4%), 328 (3), 303 (1, M − CO_2Me), 245 (3, M − CCl_3), 201 (6 M − H_2COCCl_3), 185 (1), 170 (2), 158 (1), 143 (1), 130 (100, $ArCH_2^{\bullet+}$), 103 (3), 77 (3) and 36 (14).

Methyl 1,3,4,5,6,7-*Hexahydro*-6,7-*dioxopyrrolo*[4,3,2-fg][3]-*benzazocine*-4-*carboxylate* **30**.—A solution of *N*-(trichloroacetyl)tryptophan methyl ester **29** (200 mg, 0.55 mmol) in (95:5) acetonitrile–water (100 cm^3) was irradiated for 1 h. The dark orange solution was evaporated and the residue was chromatographed (6% MeOH–CH_2Cl_2) to give the *title compound* **30** (123 mg), which coeluted with a dark red chromophore which was removed by rechromatography using a high silica-to-compound ratio. The final yield of compound **30** was 112 mg (75%) as a fluorescent, dark yellow crystalline solid, m.p. 256–258 °C with evolution of gas (Found: C, 61.5; H, 4.4; N, 10.1. $C_{14}H_{12}N_2O_4$ requires C, 61.8; H, 4.4; N, 10.3%); $[\alpha]_D$ −302 (*c* 0.500 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3689, 3472 (indole NH), 1746 (ester C=O), 1679 (amide C=O), 1648, 1603, 1437, 1343, 1287, 1233, 1123, 998, 805 and 710; λ_{max}(MeOH)/nm 205 (log ε 4.39), 235 (4.03) and 360 (3.65); δ_H(250 MHz; [$^2H_6$]acetone) 3.42 (1 H, dd, *J* 12.2 and 16.7, 3-H), 3.63 (1 H, d, *J* 16.7, 3-H), 3.80 (3 H, s, CO_2Me), 4.90 (1 H, m, 4-H), 7.22 (1 H, t, *J* 7.7, 9-H), 7.37 (1 H, br d, *J* 7.2, 8-H), 7.51 (1 H, s, 2-H), 7.72 (1 H, dd, *J* 1.2 and 8.0, 10-H), 7.80 (1 H, br d, 5-H) and 10.97 (1 H, br s, 1-H); *m/z* 272 (M^+, 68%), 244 (36, M − CO), 185 (52, M − CO − CO_2Me), 170 (53), 158 (91), 145 (18), 144 (22), 130 (84), 129 (100), 43 (41) and 28 (78).

N-(*Trichloroacetyl*)*tryptophanol* **31**.—To a suspension of *N*-(trichloroacetyl)tryptophan methyl ester **29** (300 mg, 0.83 mmol) in ethanol (12 cm^3) at 0 °C was added a solution of sodium borohydride (156 mg, 4.1 mmol) in water (3 cm^3). After 48 h the reduction was still incomplete but dehalogenation of the trichloromethyl group was beginning to predominate so the reaction was halted. The mixture was evaporated to a minimum volume, diluted with water, saturated with sodium chloride and extracted with dichloromethane. The combined extracts were dried over sodium sulfate and evaporated and the residue was chromatographed (4% MeOH–CH_2Cl_2) to give the *title compound* **31** (48 mg, 17%) as a resin (Found: M^+, 334.0047. $C_{13}H_{13}Cl_3N_2O_2$ requires M, 334.0043); $[\alpha]_D$ −26.2 (*c* 0.706 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3479 (indole NH), 3417 (amide NH), 3025, 3011, 2934, 1708 (C=O), 1510, 1458, 1442, 1420, 1339, 1092, 1036, 1012, 900, 854 and 824 (CCl_3); δ_H(250 MHz; [$^2H_6$]acetone) 3.07 (1 H, dd, *J* 6.5 and 14.6, ArC*H*H), 3.15 (1 H, dd, *J* 7.4 and 14.6, ArCH*H*), 3.70 (2 H, m, CH_2OH), 4.21 (1 H, m, C*H*NHCO), 7.02 (1 H, t, *J* 7.6, 5-H), 7.09 (1 H, t, *J* 7.6, 6-H), 7.21 (1 H, s, 2-H), 7.37 (1 H, d, *J* 8.1, 7-H), 7.70 (1 H, d, *J* 7.9, 4-H), 7.87 (1 H, br s, CHN*H*CO) and 10.10 (1 H, br s, 1-H); *m/z* 334 (M^+, 4%), 300 (1), 217 (1, M − CCl_3), 216 (1), 197 (1), 173 (16, M − $H_2NCOCCl_2$), 130 (100, $ArCH^{\bullet+}$), 58 (19), 43 (54), 36 (16) and 31 (48).

7-*Chloro*-1,3,4,5,6,7-*hexahydro*-6-*oxo*-7,4-(*epoxymethano*)*pyrrolo*[4,3,2-fg][3]*benzazocine* **32**.—A solution of *N*-(trichloroacetyl)tryptophanol **31** (86 mg, 0.26 mmol) in acetonitrile (50 cm^3) was irradiated for 1 h. The resulting opaque, dark green solution was evaporated and the residue was chromatographed (8% MeOH–CH_2Cl_2) to give the *title compound* **32** (24 mg, 36%) as an amorphous, highly insoluble tan solid (Found: M^+, 262.0503. $C_{13}H_{11}ClN_2$ requires M, 262.0509); $[\alpha]_D$ +67.1 (*c* 0.216 in MeOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 1684 (C=O), 1640, 1450, 1417 and 1348; δ_H(250 MHz; [$^2H_6$]acetone) 3.27 (1 H, d, *J* 16.7, 3-H), 3.59 (1 H, dd, *J* 7.9 and 16.7, 3-H), 4.14 (2 H, d, 4- and 12-H), 4.30 (1 H, d, 12-H), 7.07 (1 H, t, *J* 7.7, 9-H), 7.22 (1 H, s, 2-H), 7.40 (1 H, d, *J* 7.9, 10-H), 7.47 (1 H, d, *J* 7.5, 8-H) and 7.81 (1 H, br s, 5-H); *m/z* 262 (M^+, 69%), 227 (12, M − Cl), 219 (5, M − CONH), 199 (12), 192 (39), 184 (100, M − CONH − Cl), 169 (14), 164 (7), 156 (21), 154 (21), 129 (42), 115 (9, $Ar^{\bullet+}$), 110 (4), 92 (13) and 77 (19).

Trichloro-N-[2′-(*indol*-3-*yl*)*ethyl*]*acetamide* **33**.—To a solution of tryptamine (5.0 g, 31.2 mmol) and pyridine (2.5 cm^3, 31.2 mmol) in dry dichloromethane (50 cm^3) at 0 °C was added dropwise trichloroacetyl chloride (3.8 cm^3, 34.3 mmol). The brown solution was stirred at ambient temperature for 1 h, and then was evaporated to leave a yellow-brown solid. This was purified by chromatography (CH_2Cl_2) to give the *title compound* **33** (9.31 g, 98%) as a crystalline solid, m.p. 102–103 °C (Found: C, 47.1; H, 3.45; N, 9.0. $C_{12}H_{11}Cl_3N_2O$ requires C, 47.2; H, 3.6; N, 9.2%); ν_{max}(Nujol)/cm^{-1} 3412 (indole NH), 3351 (amide NH), 1715 (C=O), 1695, 1526, 1257, 1223, 1208, 825, 807 and 742; δ_H(270 MHz; $CDCl_3$) 3.09 (2 H, td, *J* 5.9 and 0.7, 1′-H_2), 3.70 (2 H, dt, *J* 6.6 and 5.9, 2′-H_2), 6.78 (1 H, br s, CH_2NHCO), 7.08 (1 H, d, *J* 2.4, 2-H), 7.16 (1 H, td, *J* 7.1 and 1.2, 5-H), 7.24 (1 H, td, *J* 6.8 and 1.2, 6-H), 7.40 (1 H, d, *J* 8.1, 7-H), 7.64 (1 H, d, *J* 7.8, 4-H) and 8.09 (1 H, br s, 1-H); *m/z* 304 (M^+, 3%), 149 (6), 144 (9), 143 (38), 131 (11), 130 (100, $ArCH_2^{\bullet+}$), 84 (6) and 77 (8).

Irradiation of Trichloro-N-[2′-(*indol*-3-*yl*)*ethyl*]*acetamide* **33** *in Methanolic Acetonitrile*.—A solution of trichloro-*N*-[2′-(indol-3-yl)ethyl]acetamide **33** (0.10 g, 0.327 mmol) in 20% methanol–acetonitrile (50 cm^3) was irradiated for 30 min. The green-brown solution was evaporated, and the residue was purified by chromatography (5% MeOH–CH_2Cl_2) to give, firstly, 1,3,4,5,6,7-*hexahydro*-7,7-*dimethoxy*-6-*oxopyrrolo*[4,3,2-fg][3]*benzazocine* **34** (0.036 g, 42%) as a yellow solid, m.p. 244–246 °C (decomp.) (Found: M^+, 260.1161. $C_{14}H_{16}N_2O_3$ requires M, 260.1161); $\nu_{max}(CHCl_3)/cm^{-1}$ 3479 (indole NH),

1660 (C=O), 1344, 1223, 1173, 1123, 1089, 666 and 559; λ_{max}(MeOH)/nm 297 (log ε 3.76); δ_H(270 MHz; $CDCl_3$) 3.03–3.09 (1 H, m, 3-H), 3.19 (3 H, s, OMe), 3.21–3.29 (1 H, m, 3-H), 3.42–3.49 (1 H, m, 4-H), 3.56 (3 H, s, OMe), 4.08–4.17 (1 H, m, 4-H), 5.76 (1 H, br s, 5-H), 7.05 (1 H, d, *J* 2.0, 2-H), 7.20 (1 H, t, *J* 7.7, 9-H), 7.35 (1 H, dd, *J* 8.0 and 1.0, 8-H), 7.64 (1 H, dd, *J* 7.5 and 1.0, 10-H) and 8.12 (1 H, br s, 1-H); *m/z* 260 (M^+, 22%), 228 (65), 213 (44), 201 (44), 169 (96), 154 (44), 153 (100) and 129 (51).

This was followed by 1,3,4,5,6,7-*hexahydro*-6,7-*dioxopyrrolo*[4,3,2-fg][3]*benzazocine* **35** (0.008 g, 12%), which was isolated as a golden yellow solid, m.p. 274–278 °C (decomp.) (Found: C, 67.1; H, 4.8; N, 12.8. $C_{12}H_{10}N_2O_2$ requires C, 67.3; H, 4.71; N, 13.1%); ν_{max}($CHCl_3$)/cm^{-1} 3290 (indole NH), 1658 (amide and ketone C=O), 1607, 1345, 1251, 1033 and 743; λ_{max}(MeOH)/nm 237 (log ε 3.50), 331infl and 353 (4.13); δ_H(270 MHz; [$^2H_6$]acetone) 3.10–3.16 (1 H, m, 3-H), 3.20–3.32 (2 H, m, 3- and 4-H), 3.71–3.83 (1 H, m, 4-H), 7.20 (1 H, t, *J* 7.5, 9-H), 7.35 (1 H, dd, *J* 7.3 and 1.2, 8-H), 7.43 [1 H, s (with multiple fine splitting), 2-H], 7.45–7.54 (1 H, br s, 5-H), 7.69 (1 H, dd, *J* 8.1 and 1.2, 10-H) and 7.86 (1 H, br s, 1-H); *m/z* 214 (M^+, 33%), 186 (33), 158 (22), 157 (15), 143 (17), 130 (41), 129 (100) and 115 (18).

Irradiation of Trichloro-N-[2′-(*indol*-3-*yl*)*ethyl*]*acetamide* **33** *in Aqueous Acetonitrile*.—A solution of trichloro-*N*-[2′-(indol-3-yl)ethyl]acetamide **33** (0.20 g, 0.654 mmol) in 20% water–acetonitrile (100 cm^3) was irradiated for 45 min. The green-brown solution was evaporated to ~20 cm^3 and then water (~50 cm^3) was added. The green-brown suspension was thoroughly extracted with dichloromethane (4 × 100 cm^3), the combined green-yellow extracts then being washed with brine (50 cm^3) which removed much of the green colour to leave a golden yellow solution. The brine solution was then re-extracted with dichloromethane (3 × 30 cm^3), and all the combined extracts were dried ($MgSO_4$) before evaporation to leave a golden brown solid. This was purified by chromatography (5% MeOH–CH_2Cl_2) to give 1,3,4,5,6,7-hexahydro-6,7-dioxopyrrolo[4,3,2-*fg*][3]benzazocine **35** (0.089 g, 64%) as a golden yellow solid, m.p. 275–278 °C (decomp.) data given above.

2-*Chloro*-3-*phenylpropionic Acid*.—An LDA solution was prepared from diisopropylamine (1.0 cm^3, 0.74 g, 7.3 mmol) and butyllithium (4.7 cm^3 of a 1.55 mol dm^{-3} solution in hexanes, 7.3 mmol) in THF (5 cm^3) at −20 °C. To this was added a solution of 3-phenylpropionic acid (0.50 g, 3.3 mmol) in THF (2 cm^3) at such a rate as not to allow the temperature to exceed 0 °C. When the addition was complete the mixture was stirred for 30 min at 0 °C, then taken to −78 °C, where dry tetrachloromethane (0.35 cm^3, 0.56 g, 3.7 mmol) in THF (1 cm^3) was added dropwise during 5 min, during which the reaction mixture went from pale pink to green and finally dark brown. The reaction was allowed to come to room temperature and after 1 h was poured into 0.5 mol dm^{-3} hydrochloric acid (40 cm^3, 20 mmol) and extracted with ether. The combined organic layer was dried over sodium sulfate and evaporated and the residual crude product was purified by chromatography [1% AcOH–Et_2O; visualisation with cerium(IV) sulfate spray reagent] to give the title compound (0.55 g, 89%) as a brown oil used without further purification: ν_{max}(film)/cm^{-1} 3000br (CO_2H), 1724 (C=O), 1631, 1606, 1497, 1455, 1288, 1259, 1206, 1080, 1032, 954, 918, 832, 809, 747 and 700; δ_H(60 MHz; $CDCl_3$) 3.30 (2 H, m, PhCH_2), 4.53 (1 H, t, *J* 7.2, ClC*H*CO_2H), 7.33 (5 H, s, Ph) and 10.58 (1 H, br s, CO_2H).

N-(2-*Chloro*-3-*phenylpropionyl*)*tryptophan Methyl Ester* **37**.—A solution of 2-chloro-3-phenylpropionyl chloride **36** [prepared from the above acid (0.55 g, 3.0 mmol) and thionyl chloride (5 cm^3); 70 °C; 45 min] in dichloromethane (2.5 cm^3) was added dropwise during 15 min to a vigorously stirred two-phase system of tryptophan methyl ester (0.65 g, 3.0 mmol) in dichloromethane (5 cm^3) and sodium hydrogen carbonate (0.50 g, 6.0 mmol) in water (5 cm^3) at 0 °C. The reaction mixture was kept for an additional 1 h at 0 °C, then poured into water and extracted with dichloromethane. The combined organic layer was dried over magnesium sulfate and evaporated to leave a resinous, light brown product which was chromatographed (4% Et_2O–CH_2Cl_2) to give the *title compound* **37** (1:1 mixture of diastereoisomers) (0.83 g, 73%) as an amber resin which resisted attempts at crystallisation (Found: M^+, 384.1248. $C_{21}H_{21}ClN_2O_3$ requires M, 384.1241); $[\alpha]_D$ +3.2 (*c* 1.00 in MeOH); ν_{max}($CHCl_3$)/cm^{-1} 3479 (indole NH), 3407 (amide NH), 3031, 3011, 2955, 1743 (ester C=O), 1670 (amide C=O), 1520, 1457, 1439, 1421, 1362, 1182, 1093, 1012 and 845; λ_{max}(MeOH)/nm 216 (log ε 4.55) and 277 (3.72); δ_H(250 MHz; [^2H]acetone) (both isomers) 3.05 (2 H, dd, *J* 7.6 and 13.9, COClCHCH_2), 3.18 (2 H, d, *J* 6.2, indole-CH_2), 3.25 (2 H, d, *J* 6.0, indole-CH_2), 3.32 (1 H, dd, *J* 6.9 and 13.9, COClCHC*H*H), 3.34 (1 H, dd, *J* 6.3 and 13.9, COClCHC*H*H), 3.60 (3 H, s, CO_2Me), 3.63 (3 H, s, CO_2Me), 4.68 (2 H, m, COClC*H*CH_2), 4.78 (2 H, m, C*H*NHCO), 6.88 (1 H, s, 2-H), 6.97–7.53 (uninterpretable collection of peaks comprising signals for 2-, 4-, 5-, 6- and 7-H, and Ph), 7.63 (2 H, br s, CHN*H*CO), 10.05 (1 H, br s, 1-H) and 10.11 (1 H, br s, 1-H); *m/z* 384 (M^+, 6%), 325 (1, M − CO_2Me), 201 (27, M − H_2COCHClCH_2Ph), 149 (7), 142 (6), 130 (100, Ar$CH_2^{\bullet+}$), 120 (6), 103 (8), 91 (29, Ph$CH_2^{\bullet+}$) and 59 (26).

Irradiation of N-(2-*Chloro*-3-*phenylpropionyl*)*tryptophan Methyl Ester* **37**.—A solution of *N*-(2-chloro-3-phenylpropionyl)tryptophan methyl ester **37** (228 mg, 0.59 mmol) in acetonitrile (100 cm^3) was irradiated for 75 min. A second trial (203 mg, 0.54 mmol) was carried out and the two were combined (total 431 mg, 1.12 mmol). The solvent was evaporated off and the residue was chromatographed (3% MeOH–CH_2Cl_2) to give, first, (7S)-*methyl* 7-*benzyl* 1,3,4,5,6,7-*hexahydro*-6-*oxopyrrolo*[4,3,2-fg][3]*benzazocine*-4-*carboxylate* **38** (48 mg, 12%) as crystals, m.p. 219–221 °C (Found: C, 72.6; H, 5.7; N, 8.1. $C_{21}H_{20}N_2O_3$ requires C, 72.4; H, 5.8; N, 8.0%); $[\alpha]_D$ −130 (*c* 0.27 in MeOH); ν_{max}($CHCl_3$)/cm^{-1} 3478 (indole NH), 3371 (amide NH), 3030, 3009, 2957, 1744 (ester C=O), 1665 (amide C=O), 1497, 1456, 1438, 1396, 1344, 1183, 1007 and 933; λ_{max}(MeOH)/nm 203 (log ε 4.47) and 283 (3.71); δ_H(250 MHz; [$^2H_6$]acetone) 3.27 (1 H, dd, *J* 4.6 and 13.5, PhC*H*H), 3.50 (1 H, dd, *J* 3.9 and 16.3, 3-H), 3.68 (1 H, dd, *J* 9.4 and 13.0, PhCH*H*), 3.77 (3 H, s, CO_2Me), 4.08 (1 H, dd, *J* 8.4 and 16.3, 3-H), 4.73 (1 H, dd, *J* 3.9 and 8.4, 4-H), 5.00 (1 H, dd, *J* 4.6 and 9.8, 7-H), 6.00 (1 H, br s, 5-H), 7.02–7.45 (uninterpretable collection of peaks comprising signals for 2-, 8-, 9- and 10-H, and Ph) and 10.16 (1 H, br s, 1-H); *m/z* 348 (M^+, 100%), 289 (12, M − CO_2Me), 259 (16), 257 (22, M − PhCH_2), 244 (25), 234 (54), 232 (33), 229 (34), 225 (18), 217 (30), 201 (26), 197 (16), 170 (41), 154 (31), 130 (89), 115 (27, indole$^{\bullet+}$) and 91 (40, Ph$CH_2^{\bullet+}$). Continued chromatography gave (7R)-*methyl* 7-*benzyl*-1,3,4,5,6,7-*hexahydro*-6-*oxopyrrolo*[4,3,2-fg][3]*benzazocine*-4-*carboxylate* **39** (137 mg, 35%) as a semi-crystalline solid (Found: C, 72.4; H, 5.9; N, 7.9); $[\alpha]_D$ +13.6 (*c* 1.00 in MeOH); ν_{max}($CHCl_3$)/cm^{-1} 3478 (indole NH), 3396 (amide NH), 3029, 3009, 2955, 1736 (ester C=O), 1666 (amide C=O), 1497, 1456, 1437, 1417, 1346, 1286, 1237, 1173, 1105, 1016 and 814; λ_{max}(MeOH)/nm 203 (log ε 4.50) and 283 (3.75); δ_H(250 MHz; [$^2H_6$]acetone) 3.31 (1 H, dd, *J* 5.6 and 13.6, PhC*H*H), 3.44 (3 H, s, CO_2Me), 3.50 (1 H, dd, *J* 8.6 and 15.2, 3-H), 3.67 (1 H, dd, *J* 8.6 and 13.8, PhCH*H*), 3.82 (1 H, dd, *J* 11.2 and 15.2, 3-H), 4.19 (1 H, m, 4-H), 4.94 (1 H, dd, *J* 5.6 and

8.5, 7-H), 6.53 (1 H, br d, *J* 6.7, 5-H), 7.00–7.42 (uninterpretable collection of peaks comprising signals for 2-, 8-, 9- and 10-H, and Ph) and 10.10 (1 H, br s, 1-H); *m/z* 348 (M^+, 100%), 289 (6, M − CO_2Me), 261 (9), 257 (21, M − $PhCH_2$), 244 (10), 234 (38), 232 (30), 229 (58), 225 (9), 217 (12), 197 (11), 170 (50), 169 (34), 154 (20), 142 (16), 130 (14), 115 (24, indole$^{\bullet+}$), 69 (24), 57 (34) and 43 (30).

5-(*Indol-3′-yl*)*pentanoic Acid* **40**.—Into a 3-necked flask equipped with overhead stirrer and Dean–Stark trap were placed indole (20 g, 0.171 mol), δ-valerolactone (19.66 g, 0.196 mol) and potassium hydroxide pellets (85% reagent; 16.90 g, 0.256 mol), together with *p*-cymene (100 cm^3). The mixture was stirred and heated to reflux, and this temperature was maintained until production of water had ceased (96 h). After this time the mixture was allowed to cool, producing a brown solution and a pale brown gum. Water (~50 cm^3) was added, and the mixture was stirred until the gummy substance had dissolved. The aqueous phase was separated and washed with light petroleum (3 × 30 cm^3), the combined organic extracts furnishing, on evaporation, mainly unchanged indole (5.56 g). The aqueous phase was cautiously acidified with conc. hydrochloric acid, which produced a red-brown oil. The mixture was kept below 4 °C for 2 days, after which time the oil had solidified. The solid material was filtered from the aqueous phase and washed with water (2 × 30 cm^3). The solid was dissolved in ether, to give a red solution and an oily residue. The ether layer was separated, washed with water (3 × 50 cm^3) which removed much of the red colour, and then dried ($MgSO_4$). The ether solution was evaporated to approximately half its volume, and was then kept at 0–4 °C overnight. Crystallisation was completed by cooling in a solid CO_2 bath, the product was filtered, and the solid was washed with a small quantity of cold ether. Concentration of the recrystallisation filtrates afforded further crops of the title compound **40** (total yield 15.19 g, 41%) as an off-white powdery solid, m.p. 104–105 °C (lit.,[16] 105–107 °C) (Found: C, 72.0; H, 7.05; N, 6.35. Calc. for $C_{13}H_{15}NO_2$: C, 71.9; H, 7.0; N, 6.45%); ν_{max}(Nujol)/cm^{-1} 3500–2500 (OH), 3427 (indole NH), 1690, 1409, 1299, 1258, 1200, 1089 and 736; δ_H(20 MHz; $CDCl_3$) 1.76 (4 H, m, 3- and 4-H_2), 2.40 (2 H, t, *J* 7.9, 2-H_2), 2.79 (2 H, t, *J* 7.4, 5-H_2), 6.97 (1 H, s, 2′-H), 7.14 (2 H, m, 5′- and 6′-H), 7.35 (1 H, d, *J* 7.1, 7′-H), 7.59 (1 H, d, *J* 7.5, 4′-H) and 7.90 (1 H, br s, 1′-H); *m/z* 217 (M^+, 33%), 158 (7), 144 (11), 130 (100, $ArCH_2^{\bullet+}$), 103 (12) and 77 (15).

5-(*Indol-3′-yl*)-NN-*dimethylpentanamide* **41**.—To a solution of 5-(indol-3′-yl)pentanoic acid **40** (1.0 g, 4.60 mmol) and triethylamine (0.50 g, 4.94 mmol) in THF (20 cm^3) at 0 °C under nitrogen was added isobutyl chloroformate (0.70 g, 5.13 mmol). The cloudy mixture was stirred at 0 °C for 30 min, after which time it was added dropwise to a solution of dimethylamine in industrial methylated spirits (33% solution; 20 cm^3), also at 0 °C. The mixture was allowed to warm to ambient temperature, whereupon a yellow solution was obtained. This was diluted with water (50 cm^3) and extracted with dichloromethane (3 × 50 cm^3), the combined extracts being washed with water (2 × 100 cm^3), dried ($MgSO_4$), and evaporated to give a solid. The solid was recrystallised from dichloromethane–light petroleum to give the *title compound* **41** (0.92 g, 82%) as a granular solid, m.p. 133–134 °C (Found: C, 73.5; H, 8.35; N, 11.4. $C_{15}H_{20}N_2O$ requires C, 73.7; H, 8.25; N, 11.5%); ν_{max}(film)/cm^{-1} 3192 (indole NH), 1633 (C=O), 1413, 1330, 1232, 1152, 1081, 778, 748 and 727; δ_H(200 MHz; $CDCl_3$) 1.76 (4 H, m, 3- and 4-H_2), 2.35 (2 H, t, *J* 7.2, 2-H_2), 2.79 (2 H, t, *J* 7.4, 5-H_2), 2.94 (3 H, s, NMe), 2.97 (3 H, s, NMe), 6.98 (1 H, d, *J* 2.7, 2′-H), 7.13 (2 H, m, 5′- and 6′-H), 7.34 (1 H, d, *J* 7.4, 7′-H), 7.60 (1 H, d, *J* 7.4, 4′-H) and 8.08 (1 H, br s, 1′-H); *m/z* 244 (M^+, 26%), 199 (5), 157 (10), 143 (22), 130 (100, $ArCH_2^{\bullet+}$), 117 (13), 87 (18), 72 (15) and 45 (16).

5-[1′-(tert-*Butoxycarbonyl*)*indol-3′-yl*]-NN-*dimethylpentanamide* **42**.—To a suspension of 5-(indol-3′-yl)-*NN*-dimethylpentanamide **41** (0.40 g, 1.64 mmol) in dry acetonitrile (10 cm^3) were added di-*tert*-butyl dicarbonate (0.54 g, 2.46 mmol) and 4-(dimethylamino)pyridine (DMAP) (0.020 g, 0.164 mmol). The colourless suspension was stirred at ambient temperature for 15 h to give a clear, pale yellow solution, which was then evaporated to leave a yellow-brown gum. This was purified by chromatography (CH_2Cl_2) to give the *title compound* **42** (0.56 g, 100%) as a very pale yellow, crystalline solid, m.p. 117–118 °C (Found: C, 69.7; H, 8.3; N, 8.2. $C_{20}H_{28}N_2O_3$ requires C, 69.7; H, 8.2; N, 8.1%); ν_{max}(Nujol)/cm^{-1} 1732 (carbamate C=O), 1650 (amide C=O), 1276, 1209, 1161, 1091, 1034, 765 and 750; δ_H(270 MHz; $CDCl_3$) 1.66 (9 H, s, Bu^t), 1.76 (4 H, quintet, *J* 3.7, 3- and 4-H_2), 2.35 (2 H, m, 2-H_2), 2.71 (2 H, m, 5-H_2), 2.94 (3 H, s, NMe), 2.98 (3 H, s, NMe), 7.19–7.33 (2 H, m, 5′- and 6′-H), 7.35 (1 H, s, 2′-H), 7.51 (1 H, dd, *J* 7.6 and 1.2, 4′-H) and 8.11 (1 H, d, *J* 8.1, 7′-H); *m/z* 344 (M^+. 43%), 244 (85), 199 (27), 143 (33), 130 (100, $ArCH_2^{\bullet+}$), 117 (31), 87 (31) and 57 (72).

5-[1′-(tert-*Butoxycarbonyl*)*indol-3′-yl*]-2-*chloro*-NN-*dimethylamide* **43**.—A solution of lithium isopropylcyclohexylamide (LiICA) was prepared by addition of butyllithium (1.5 mol dm^{-3} solution in hexanes; 0.60 cm^3, 0.087 mmol) to *N*-isopropylcyclohexylamine (145 mm^3, 0.087 mmol) in THF (20 cm^3) at −20 °C under nitrogen, and the solution was allowed to warm to 0 °C for 5 min before being cooled to −78 °C. A solution of 5-[1′-(*tert*-butoxycarbonyl)indol-3′-yl]-*NN*-dimethylpentanamide **42** (0.20 g, 0.058 mmol) in THF (5 cm^3) was added dropwise to the LiICA solution. After a further 10 min, the mixture was allowed to warm slowly to −20 °C, to give a clear orange solution. This was cooled again to −78 °C, and then added *via* catheter to a solution of dry tetrachloromethane (6 cm^3) in THF (10 cm^3), also at −78 °C under nitrogen. The solution was stirred at −78 °C for a further 10 min, and was then allowed to warm slowly to ambient temperature, to give a pale yellow solution. After a further 20 min, acetic acid (0.5 cm^3) was added, and the resulting solution was diluted with water (30 cm^3) and extracted with dichloromethane (3 × 40 cm^3). The combined extracts were dried ($MgSO_4$), evaporated, and purified by chromatography (2% MeOH–CH_2Cl_2) to give the *title compound* **43** (0.100 g, 45%) as a pale brown oil (Found: M^+, 378.1710. $C_{20}H_{27}ClN_2O_3$ requires M, 378.1710); ν_{max}(film)/cm^{-1} 1732 (carbamate C=O), 1661 (amide C=O), 1452, 1371, 1256, 1157, 1091 and 748; δ_H(270 MHz; $CDCl_3$), 1.68 (9 H, s, Bu^t), 1.72–1.92 (2 H, m, 4-H_2), 2.01–2.18 (2 H, m, 3-H_2), 2.73–2.82 (2 H, m, 5-H_2), 2.98 (3 H, s, NMe), 3.07 (3 H, s, NMe), 4.44 (1 H, t, *J* 7.6, 2-H), 7.21–7.35 (2 H, m, 5′- and 6′-H), 7.39 (1 H, s, 2′-H), 7.52 (1 H, d, *J* 7.3, 4′-H) and 8.14 (1 H, br d, *J* 8.1, 7′-H); *m/z* 378 (M^+, 13%), 278 (19), 170 (40), 143 (76), 130 (31, $ArCH_2^{\bullet+}$), 72 (22), 57 (100) and 41 (20).

2-*Chloro*-5-(*indol-3′-yl*)-NN-*dimethylpentanamide* **44**.—To a solution of 5-[1′-(*tert*-butoxycarbonyl)indol-3′-yl]-2-chloro-*NN*-dimethylpentanamide **43** (0.070 g, 0.185 mmol) in dichloromethane (15 cm^3) was added dropwise trifluoroacetic acid (TFA) (200 mm^3). The pale purple solution was stirred at ambient temperature for 1 h, and was then evaporated under reduced pressure to leave a purple oil. This was purified by chromatography (1% MeOH–CH_2Cl_2) to give the *title compound* **44** (0.038 g, 73%) as an oil (Found: M^+, 278.1186. $C_{15}H_{19}ClN_2O$ requires M, 278.1186); ν_{max}(film)/cm^{-1} 3470 (indole NH), 1655 (amide C=O), 1490, 1454, 1417 and 1338; λ_{max}(MeOH)/nm 290 (log ε 3.17), 320infl and 340infl; δ_H(270 MHz; $CDCl_3$) 1.74–1.93 (2 H, m, 4-H_2), 1.98–2.19 (2 H, m, 3-

H_2), 2.82 (2 H, t, *J* 7.4, 5-H_2), 2.96 (3 H, s, NMe), 3.01 (3 H, s, NMe), 4.40 (1 H, dd, *J* 7.6 and 6.3, 2-H), 7.00 (1 H, d, *J* 2.0, 2′-H), 7.10 (1 H, td, *J* 7.5 and 1.0, 5′-H), 7.18 (1 H, td, *J* 7.5 and 1.1, 6′-H), 7.35 (1 H, d, *J* 8.0, 7′-H), 7.59 (1 H, d, *J* 8.0, 4′-H) and 8.20 (1 H, br s, 1′-H); *m/z* 278 (M^+, 19%), 170 (40), 168 (17), 143 (76), 130 (31, $ArCH_2^{\bullet+}$), 72 (22), 57 (100) and 41 (20).

6-(*Indol*-3′-*yl*)*hexanoic Acid* **45**.—To a solution of oxepan-2-one (11.1 cm^3, 11.4 g, 0.10 mol) in *p*-cymene (40 cm^3) was added potassium hydroxide (7.9 g of 85% reagent, 0.12 mol) and the mixture was heated to reflux in a flask surmounted by a Dean–Stark trap. After some water (~0.5 cm^3) had been collected, the reaction mixture was cooled to room temperature and indole (5.86 g, 0.050 mol) was added. The mixture was then reheated until production of water had apparently stopped (72 h). The mixture was filtered, and from the filtrate was recovered unchanged indol (2.92 g). The filtered solid was dissolved in water, washed with ether, and acidified to pH 5 with dil. hydrochloric acid. The resulting murky suspension was extracted with ether and the organic layer was back-extracted with water, then dried over sodium sulfate. Evaporation gave a yellow solid with a skatole-like odour and which was shown by NMR spectroscopy to be mainly the title compound **45**, although isomeric 6-(*indol*-1′-*yl*)*hexanoic acid* was a minor impurity, much of which could be removed at 85 °C and 3×10^{-2} mmHg as a foul-smelling yellow oil. The remaining solid was crystallised from chloroform to give title compound **45** (3.21 g, 28%, or 55% based on consumed indole) as a solid, m.p. 139–142 °C (lit.,[16] 143–144 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 3600–2400 (CO_2H dimer), 3482 (NH), 3061, 3009, 2935, 2859, 1709 (C=O), 1457, 1418, 1337, 1277, 1191, 1089, 1040, 1011 and 925; λ_{max}(MeOH)/nm 223 (log ε 4.51) and 283 (3.73); δ_H(270 MHz; $CDCl_3$) 1.44 (2 H, m, 4-H_2), 1.70 (4 H, m, 3- and 5-H_2), 2.35 (2 H, t, *J* 7.4, 2-H_2), 2.75 (2 H, t, *J* 7.4, 6-H_2), 6.95 (1 H, s, 2′-H), 7.09 (1 H, t, *J* 7.3, 5′-H), 7.17 (1 H, t, *J* 7.5, 6′-H), 7.33 (1 H, d, *J* 8.2, 7′-H), 7.58 (1 H, d, *J* 7.8, 4′-H) and 7.88 (1 H, br s, 1′-H); *m/z* 231 (M^+, 32%), 156 (4), 144 (3), 143 (3), 130 (100, $ArCH_2^{\bullet+}$), 117 (7), 103 (5), 91 (4) and 77 (6).

6-(*Indol*-3′-*yl*)-NN-*dimethylhexanamide* **46**.—To a solution of 6-(indol-3′-yl)hexanoic acid **45** (100 mg, 0.43 mmol) and triethylamine (44 mg, 0.44 mmol) in THF (5 cm^3) at 0 °C under nitrogen was added isobutyl chloroformate (59 mm^3, 62 mg, 0.45 mmol). The clear solution immediately went cloudy and after 30 min was introduced dropwise into 10% aq. dimethylamine (10 cm^3) at 0 °C. The reaction mixture was removed from the ice bath and, once it had warmed to room temperature, was diluted with water (100 cm^3) and extracted with dichloromethane. The combined extracts were dried over sodium sulfate and evaporated, and the crude product was purified by chromatography (3% MeOH–CH_2Cl_2) to give the *title compound* **46** (90 mg, 80%) as a crystalline solid, m.p. 117–118 °C (Found: C, 74.3; H, 8.8; N, 10.7. $C_{16}H_{22}N_2O$ requires C, 74.4; H, 8.6; N, 10.8%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3481 (NH), 3007, 2934, 2858, 1631 (C=O), 1490, 1457, 1417, 1402, 1337, 1266, 1241, 1150, 1089, 1011 and 809; λ_{max}(MeOH)/nm 223 (log ε 4.53), 283 (3.74) and 291infl; δ_H(270 MHz; $CDCl_3$) 1.44 (2 H, m, 4-H_2), 1.71 (4 H, septet, *J* 7.6, 3- and 5-H_2), 2.28 (2 H, t, *J* 7.6, 2-H_2), 2.75 (2 H, t, *J* 7.6, 6-H_2), 2.92 (3 H, s, NMe), 2.96 (3 H, s, NMe), 6.95 (1 H, s, 2′-H), 7.08 (1 H, t, *J* 7.5, 5′-H), 7.16 (1 H, t, *J* 7.6, 6′-H), 7.33 (1 H, d, *J* 8.1, 7′-H), 7.58 (1 H, d, *J* 7.8, 4′-H) and 7.92 (1 H, br s, 1′-H); *m/z* 258 (M^+, 50%), 213 (3, M − Me_2NH), 185 (2), 156 (6), 144 (8), 143 (7), 130 (100, $ArCH_2^{\bullet+}$), 117 (12), 103 (4), 100 (11), 87 (17), 77 (5) and 72 (9).

2-*Chloro*-6-(*indol*-3′-*yl*)-NN-*dimethylhexanamide* **47**.—A solution of 6-(indol-3′-yl)-*NN*-dimethylhexanamide **46** (200 mg, 0.77 mmol) in THF (4 cm^3) was added dropwise to an LDA solution prepared from diisopropylamine (0.23 cm^3, 166 mg, 1.6 mmol) and butyllithium (1.15 cm^3 of a 1.43 mol dm^{-3} solution in hexanes, 1.6 mmol) in THF (8 cm^3) at 0 °C. After 1 h, dry tetrachloromethane (0.10 cm^3, 159 mg, 1.0 mmol) was added to the clear, light amber-coloured dianion solution, thereby causing a deep green-brown colour to develop. This was followed after 10 min by the injection of acetic acid (0.2 cm^3), and the resulting thick brown mush was diluted with water and extracted with dichloromethane. The organic layer was dried over sodium sulfate and evaporated, and the residue was chromatographed (2% MeOH–CH_2Cl_2) to give the *title compound* **47** (93 mg, 41%) as a resin (Found: M − HCl, 256.1573. $C_{16}H_{20}N_2O$ requires *m/z*, 256.1576); ν_{max}(CH-Cl_3)/cm^{-1} 3481 (NH), 3010, 2935, 2860, 1653 (C=O), 1490, 1457, 1418, 1404, 1337, 1135, 1090 and 1011; λ_{max}(MeOH)/nm 223 (log ε 4.49), 283 (3.68) and 290infl; δ_H(270 MHz; $CHCl_3$) 1.48 (2 H, m, 4-H_2), 1.74 (2 H, m, 5-H_2), 2.04 (2 H, m, 3-H_2), 2.76 (2 H, t, *J* 7.5, 6-H_2), 2.96 (3 H, s, NMe), 3.05 (3 H, s, NMe), 4.39 (1 H, t, *J* 7.2, 2-H), 6.95 (1 H, s, 2′-H), 7.08 (1 H, t, *J* 7.5, 5′-H), 7.16 (1 H, t, *J* 7.6, 6′-H), 7.33 (1 H, d, *J* 8.2, 7′-H), 7.57 (1 H, d, *J* 7.9, 4′-H) and 8.01 (1 H, br s, 1′-H); *m/z* 292 (M^+, 0.3%), 256 (33, M − HCl), 184 (100, M − HCl − $CONMe_2$), 168 (5), 156 (8), 149 (3), 143 (6), 130 (9, $ArCH_2^{\bullet+}$), 84 (9), 72 (8) and 49 (12).

Irradiation of 2-*Chloro*-6-(*indol*-3′-*yl*)-NN-*dimethylhexanamide* **47**.—A solution of 2-chloro-6-(indol-3′-yl)-*NN*-dimethylhexanamide **47** (85 mg, 0.29 mmol) in acetonitrile (100 cm^3) was irradiated for 1 h. The dark burgundy-coloured solution was evaporated and the residue was chromatographed (3% MeOH–CH_2Cl_2) to give, first, 1,3,4,5,6,7-*hexahydro*-NN-*dimethylcycloocta*[cd]*indole*-7-*carboxyamide* **48** (9.5 mg, 13%) as an orange resin (Found: M^+, 256.1581. $C_{16}H_{20}N_2O$ requires M, 256.1576); $\nu_{max}(CHCl_3)/cm^{-1}$ 3480 (NH), 3007, 2934, 2860, 1636 (C=O), 1484, 1461, 1401, 1342, 1242, 1142 and 1089; λ_{max}(MeOH)/nm 206 (log ε 4.33), 226 (4.42) and 283 (3.71); δ_H(270 MHz; $CDCl_3$) 1.57 (2 H, m, 5-H_2), 1.69–1.96 (3 H, m, 4-H_2 and 6-H), 2.28 (1 H, m, 6-H), 2.69 (3 H, s, NMe), 2.91 (1 H, dd, *J* 7.6 and 15.0, 3-H), 3.02 (3 H, s, NMe), 3.25 (1 H, ABC system, *J* 7.3, 11.5 and 15.0, 3-H), 4.82 (1 H, dd, *J* 5.3 and 12.1, 7-H), 6.66 (1 H, d, *J* 7.3, 8-H), 6.90 (1 H, s, 2-H), 7.05 (1 H, t, *J* 7.8, 9-H), 7.20 (1 H, d, *J* 8.4, 10-H) and 7.95 (1 H, br s, 1-H); *m/z* 256 (M^+, 38%), 184 (100, M − Me_2NCO), 170 (27), 156 (24), 144 (16), 143 (16), 117 (24), 100 (38) and 72 (37).

This was followed by the elimination product, 6-(*indol*-3′-*yl*)-NN-*dimethylhex*-2-*enamide* **49** (15.7 mg, 21%), also as an orange resin (Found: M^+, 256.1575. $C_{16}H_{20}N_2O$ requires M, 256.1576); $\nu_{max}(CHCl_3)/cm^{-1}$ 3480 (NH), 3007, 2935, 2860, 1658, 1609 (C=O), 1490, 1457, 1417, 1401, 1338, 1265, 1244, 1143, 1090, 1011, 977, 918 and 809; λ_{max}(MeOH)/nm 220 (log ε 4.50) and 274 (3.71); δ_H(270 MHz; $CDCl_3$) 1.87 (2 H, quintet, *J* 7.3, 5-H_2), 2.28 (2 H, q, *J* 7.1, 4-H_2), 2.78 (2 H, t, *J* 7.7, 6-H_2), 2.98 (3 H, br s, NMe), 3.02 (3 H, br s, NMe), 6.23 (1 H, d, with fine splitting, *J* 15.0, 2-H), 6.91 (1 H, dt, *J* 7.1 and 15.0, 3-H), 6.96 (1 H, s, 2′-H), 7.08 (1 H, t, *J* 7.5, 5′-H), 7.17 (1 H, t, *J* 7.5, 6′-H), 7.34 (1 H, d, *J* 8.1, 7′-H), 7.57 (1 H, d, *J* 7.7, 4′-H) and 7.98 (1 H, br s, 1′-H); *m/z* 256 (M^+, 61%), 211 (10, M − Me_2NH), 194 (23), 184 (78, M − Me_2NCO), 170 (35), 156 (16), 144 (22), 143 (20), 130 (100, $ArCH_2^{\bullet+}$), 126 (15), 117 (13), 113 (44), 100 (23) and 72 (39).

Irradiation of 2-*Chloro*-5-(*indol*-3′-*yl*)-NN-*dimethylpentanamide* **44**.—A solution of 2-chloro-5-(indol-3′-yl)-*NN*-dimethylpentanamide **44** (0.030 g, 0.108 mmol) in acetonitrile (30 cm^3) was irradiated for 20 min. The brown solution was evaporated, and the residue was purified by chromatography (2% MeOH–CH_2Cl_2) to give 5-(*indol*-3′-*yl*)-NN-*dimethylpent*-2-*enamide* **50** (0.015 g, 59%) as a golden brown oil (Found: M^+, 242.1419.

$C_{15}H_{18}N_2O$ requires M, 242.1419); ν_{max}(film)/cm^{-1} 3481 (indole NH), 1659 (amide C=O), 1494, 1457, 1417, 1401 and 1149; δ_H(270 MHz; $CDCl_3$) 2.58–2.68 (2 H, m, 4-H_2), 2.73–2.82 (2 H, m, 5-H_2), 2.91 (3 H, s, NMe), 3.00 (3 H, s, NMe), 5.95–5.98 (1 H, m, 2-H), 6.25 (1 H, dt, *J* 15.1 and 1.6, 3-H), 6.99 (1 H, d, *J* 2.0, 2′-H), 7.08–7.22 (2 H, m, 5′- and 6′-H), 7.35 (1 H, d, *J* 7.7, 7′-H), 7.60 (1 H, d, *J* 8.0, 4′-H) and 7.99 (1 H, br s, 1′-H); *m/z* 242 (M^+, 20%), 170 (12), 168 (4), 131 (10), 130 (100, $ArCH_2^{\bullet+}$), 113 (8), 98 (5) and 77 (5).

Crystal Data.—Data for all structures were collected on a Nicolet R3m diffractometer, ω-scan method, graphite-monochromated Cu-Kα radiation (λ 1.541 78 Å); all data were corrected for Lorentz and polarisation factors. No absorption corrections were applied. All structures were solved by direct methods. In all cases except for compound **22** the non-hydrogen atoms were refined anisotropically. In compound **22** the ordered molecule was refined anisotropically, with protons included isotropically. The disordered molecule was refined isotropically without protons, subject to C–C, C–N and C–O distance constraints based on the ordered molecule. All amine hydrogen atoms were located from a ΔF map and were allowed to refine isotropically, subject to a distance constraints (N–H 0.98 Å). All the other hydrogen atoms were idealised (C–H 0.96 Å), assigned isotropic thermal parameters, $U(H) = 1.2\ U_{eq}(C)$, and allowed to ride on their parent carbons. Refinement was by block-cascade full-matrix least-squares. Computations were carried out on an Eclipse S140 using the SHELXTL program system.[19]*

The crystal data for compounds **13**, **15**, **21**, **22** and **35** are given in Table 1. Atomic co-ordinates for these compounds are listed in Tables 2–6.

* The bond lengths and bond angles are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by a full literature citation for this communication. For details of the deposition scheme see 'Instructions to Authors (1992),' Section 5.6.3, in the January issue.

Acknowledgements

We thank the SERC and SmithKline Beecham for a CASE Award (to A. L. B.), and the Royal Society of Chemistry for a Hickinbottom Fellowship (to C. J. M.).

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Paper 1/05782K
Received 14*th November* 1991
Accepted 6*th January* 1992