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Heteroaryl Radicals in Synthesis: Radical Cyclisation Reactions of 2-Bromoindoles

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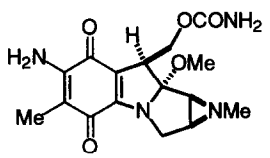
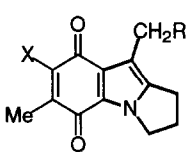
Abstract: The synthesis and radical cyclisations of 2-bromoindoles carrying an unsaturated N-alkyl group is described.

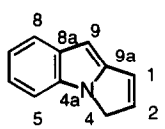
The mitomycins, mitosenes and mitosanes constitute an important class of biologically active molecules. The most important of these is mitomycin C which shows potent anti-tumour activity and is used clinically in the treatment of certain cancers. There have been many studies probing the mechanism of action of this family of compounds, in order to discover how they bind DNA[1,2] and thus their ability to affect the growth of solid tumours. It has long been known that mitomycins are not biologically potent themselves but require priming.[3-6] Indeed, it is now believed that it is a mitosene that is the reactive intermediate in this process and which binds DNA, and so the chemistry and synthesis of these compounds has also received considerable attention.[7]



Mitomycin C



General Mitosene Structure



Common pyrrolo[1,2-*a*]indole skeleton

The chemical literature contains many examples of the syntheses of these compounds by a wide variety of methodologies. For our approach, we decided to employ the new heteroaryl radical cyclisation methodology developed within our group. Whilst the generation and subsequent reactions of radicals formed from aryl halides using tri-*n*-butyltin hydride and azobisisobutyronitrile (AIBN) is now well documented[8,9] and several natural product syntheses based on aryl radical cyclisations have been reported,[10-12] little work has been published on the generation of radicals in heteroaromatic systems. Apart from our work,[13,14] there are only two reported examples of an indolyl radical: by Sundberg, in his synthesis of Iboga alkaloids,[15] where the radical is generated at the indole *C*-3 position and by Srinivasan, who also generated an indolyl radical at the C-3 position.[16] There are, however, several examples of radical addition into indolyl systems, notably by Ziegler[17] and Caddick.[18-20] As our preliminary results have shown, heteroaryl (and particularly indolyl) radicals react in a similar way to aryl radicals presumably because the lone electron is in an orbital orthogonal to the aromatic π-system and hence the nature of the π-system (π-excessive or π-deficient) has little effect on the reactivity of the radical.[13,14,21]

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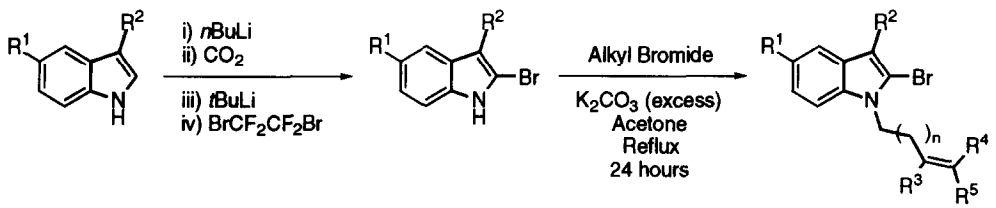
Our synthesis of the mitosene skeleton required a 2-halogen substituted indole as the main starting material. Although a number of methods exist for the preparation of such compounds, the method of Bergman[22] (based on the work of Katritzky[23,24]) gave the best yields of 2-bromoindoles. Both methods employ carbon dioxide as a temporary protecting group for the nitrogen while introducing the bromine at the *C*-2 position using 1,2-dibromotetrafluoroethane. This method worked equally well for substituted indoles, provided the substituents tolerated the reaction conditions (Scheme 1 and Table 1). (For example, reaction of indole-3-carboxylic acid failed to give any 2-bromo product, even when using an extra equivalent of butyllithium for deprotonation of the carboxylic acid).

Various methods were explored for the *N*-alkylation of the 2-bromoindoles. Using either potassium *tert*-butoxide/18-crown-6[17] or potassium hydroxide/DMSO,[25] following literature precedent, gave very poor yields of *N*-alkyl-2-bromoindoles. However simply reacting 2-bromoindole and its derivatives with a 3-5 molar excess of potassium carbonate in acetone and a similar excess of a bromoalkene (or bromoalkyne) gave the desired cyclisation precursors in good yields (Scheme 1 and Table 1). (All the alkyl bromides employed were either commercially available or prepared simply from the corresponding commercially available alcohol by reaction with carbon tetrabromide and triphenylphosphine[26]).

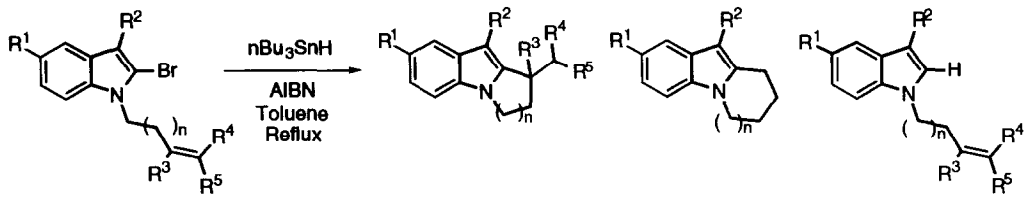


Scheme 1

Table 1: Synthesis of a Range of *N*-alkylated-2-bromoindoles.

Entry	Starting Indole			%Yield	Alkyl Bromide					%Yield
		R^1	R^2	(2-Br)		n	R^3	R^4	R^5	
1	Indole	H	H	87	4-Bromobutene	1	H	H	H	81
2	"	"	"		5-Bromopentene	2	H	H	H	64
3	"	"	"		6-Bromohexene	3	H	H	H	86
4	"	"	"		5-Bromo-2-methylpentene	1	H	Me	Me	83
5	"	"	"		4-Bromo-2-methylbutene	1	Me	H	H	72
6	"	"	"		4-Bromobutyne	1	-	-	-	61
7	"	"	"		1-TMS-4-bromobutyne	1	-	-	-	59
8	3-Methylindole	H	Me	81	4-Bromobutene	1	H	H	H	79
9	"	"	"		5-Bromopentene	1	H	H	H	74
10	5-Methoxyindole	OMe	H	68	4-Bromobutene	1	H	H	H	81
11	"	"	"		5-Bromopentene	1	H	H	H	78

The radical precursors were then subjected to normal radical reaction conditions of tri-*n*-butyltin hydride (1.2 equivalent; *ca.* 0.02M) with catalytic AIBN as the initiator in refluxing toluene for 12 hours (Scheme 2).



Scheme 2

When 5-*exo* reactions were possible, 5-membered ring products were formed exclusively, irrespective of the substituents on the carbon chain and around the double bond (Table 2; entries 12, 15 and 16). This is particularly interesting for entry 16. In the case of the simple 5-hexenyl radical, substitution at C-5 leads to formation of a mixture of cyclopentane (via 5-*exo* cyclisation) and cyclohexane (via 6-*endo* cyclisation). This is also found with aryl radical cyclisations. However in this example only the product of 5-*exo* cyclisation was detected. This may be caused by the bond angles involved in the 5-membered ring of the indole. When the chain length was extended to a *N*-pentenyl chain, a mixture of 6-*exo* cyclised product and reduction product was observed, with the cyclised product being the major one (ratio *ca.* 3.5:1); no seven-membered ring formation was observed (entry 13). Extension of the chain length even further in *N*-hexenyl-2-bromoindole (entry 14) gave no cyclised material at all, only reduced product. Alkynes have been used as acceptors in radical cyclisation reactions but usually require silylation to prevent stannylation of the triple bond. The protected alkyne underwent cyclisation but only in low yields and it was impossible to isolate any other products. This could result from decomposition of the vinylsilane product either under the reaction conditions or during the work-up. The presence of substituents around the indole ring seemed to have little effect on the radical cyclisation with good yields being obtained with substituents in both the 3- and 5- positions of the indole nucleus. (Table 2; entries 19 and 20 (3-Me substituent) and 21 and 22 (5-OMe substituent)). In both these cases, the 5-*exo* cyclisation of the *N*-butenyl precursors proceeded smoothly (entries 19 & 21) whilst the 6-*exo* cyclisation of the *N*-pentenyl precursors was always accompanied by reduction (entries 20 & 22).

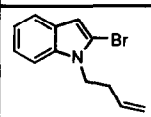
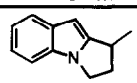
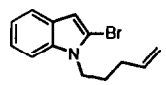
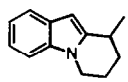
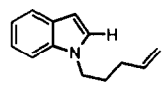
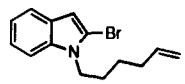
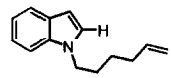
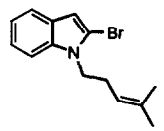
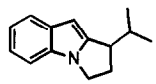
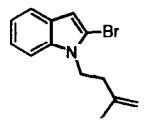
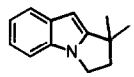
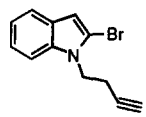
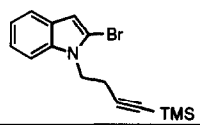
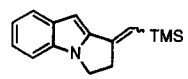
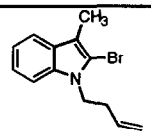
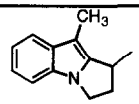
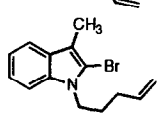
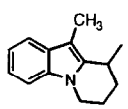
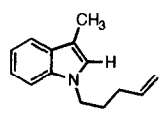
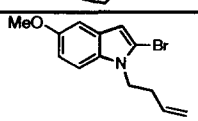
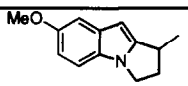
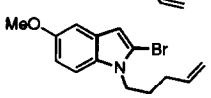
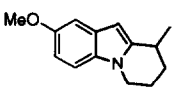
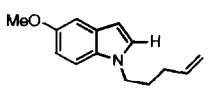
The role of the halogen in the radical precursor was also interesting. While the bromide was the generally used radical precursor, using the *ortho*-lithiation technique it was also possible to prepare the 2-chloro- (using 1,2-dichloroethane to quench the reaction) and 2-iodoindoles (using iodine). The reaction of 2-iodoindole was very rapid and could also be initiated photochemically (although giving a far more complex mixture of products, not all of which were isolated or characterised) while only starting material was obtained even after prolonged heating and repeated addition of initiator of 2-chloroindoles (mass spectrometry clearly showed the presence of chlorine still in the molecule). This would appear to reflect the relative strengths of the carbon-halogen bonds in the radical precursors, with the C-I being the weakest and thus most readily cleaved to give the indolyl radical.

In summary, we have shown that radicals at the *C*-2 position of indole can be made and used in cyclisation reactions to generate structures closely related to the mitosene skeleton and this work is being extended to the total synthesis of such systems, which will be reported in due course.

Acknowledgements:

We are grateful to the SERC and SmithKline Beecham for financial support (CASE award to APD) of this work and to Dr. Mike Fedouloff and colleagues (SB) and Dr. Sheetal Handa (KCL) for useful discussions. We also wish to thank the ULIRS Mass Spectrometry Unit and NMR service at King's College London.

Table 2: Results of Indole Radical Cyclisation Reactions.

Entry	Starting Material	Products: 5-*Exo*	6-*Endo*	Reduced	% Yield (Ratio)
12			-	-	79
13			-		74 (3.5:1)
14		-	-		78
15			-	-	71
16			-	-	73
17		-	-	-	0
18			-	-	Trace
19			-	-	73
20			-		64 (2.5:1)
21			-	-	91
22			-		96 (3:1)

Experimental:

General Details:

All reactions were carried out under argon using a vacuum/argon line dual manifold. Diethyl ether, tetrahydrofuran (THF) and toluene were distilled from sodium benzophenone ketyl immediately before use. Column chromatography was performed with silica gel (Merck 7734) using the flash chromatography technique. Thin layer chromatographic analysis was performed using plastic-backed silica plates (Merck 5735). Components were visualised by UV. All melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1605 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on either a Bruker AM 360 spectrometer operating at 360 MHz for proton and 90 MHz for carbon (KCL) or a Bruker AMX 400 instrument (SB). Chemical shift values are reported as parts per million (ppm) from an internal tetramethylsilane reference for ^{1}H spectra and from the solvent peaks for ^{13}C spectra. ^{1}H NMR spectra are recorded in the form δ_H (integration, multiplicity, coupling constants, assignment). Multiplicities are given as s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet and br: broad signal. Coupling constants (*J* values) are quoted to one decimal place with values in Hz. ^{13}C spectra are given in the form δ_C (assignment). High resolution mass spectra were performed at the Chemistry Department, King's College London using either a Kratos MS89MS with Kratos DS90 software or a Joel AX505W with Jeol complement data system.

General Preparation of 2-bromoindoles: (illustrated for 2-bromoindole)

n-Butyllithium (8.4 ml (2.5 M hexane solution), 21.00 mmol) was added dropwise to a solution of indole (2.34 g, 19.97 mmol) in THF (30 ml) under argon at -78°C. Once addition was complete, the solution was stirred at this temperature for 30 min. before bubbling carbon dioxide gas through the mixture for 10 min. The resulting clear solution was stirred for a further 10 min. before removing the solvent *in vacuo*. The white crystalline residue was dissolved in THF (30 ml) and cooled to -78 °C and *t*-butyllithium (12.4 ml (1.7M hexane solution), 21.00 mmol) slowly added. The pale yellow solution was stirred at -78°C for 1 hr. before adding 1,2-dibromotetrafluoroethane (6.52 g, 2.38 ml, 20 mmol) dropwise. The reaction mixture was stirred at -78°C for a further hour before gradually warming to room temperature. Water (5 ml) was added carefully to the reaction mixture before pouring into ammonium chloride (saturated, aqueous solution, 60 ml). The resulting solution was extracted with diethyl ether (2×100 ml) and the organic layer washed with brine (2×100 ml), dried over magnesium sulphate and evaporated. The solid residue was purified by flash chromatography (hexane:diethyl ether, 4:1) to yield the *title compound.*

2-Bromoindole: Yield: 3.47 g, 89% as a white solid; mp 81-83°C (lit.[27] mp 82 - 84°C). The product was unstable, decomposing rapidly to a dark green solid at room temperature, but could be stored in dilute solution, in diethyl ether, at -20°C in the dark. The reaction was repeated on several different scales, all with comparable yields. R_f 0.54 (hexane:diethyl ether 4:1). Found (M, $^{81}Br)^+$ 196.9671. $C_8H_7N^{81}Br$ requires 196.9664; Found (M, $^{79}Br)^+$ 194.9683. $C_8H_7N^{79}Br$ requires 194.9684; ν_{max} (nujol) 3373 (N-H), 783 & 740 (C-Br); δ_H (360 MHz; $CDCl_3$) 6.50 (1 H, dd *J* 0.7 and 1.3, C(3)**H**), 7.13 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.52 (1 H, dd, *J* 6.7, 1.1, C(4)**H**), 7.85 (1 H, br s, N**H**); δ_C (90.6MHz; $CDCl_3$) 104.8 (**C**(3)H), 108.7 (**C**(2)Br), 110.3 (**C**(7)H), 119.6 (**C**(6)H), 120.5 (**C**(4)H), 122.2 (**C**(5)H), 128.7 (**C**(3*a*)), 136.3 (**C**(7*a*)); *m/z* 197.0 [(M, $^{81}Br)^+$, 98.4%], 195.0 [(M, $^{79}Br)^+$, 100%], 116.1 [(M–Br)$^+$, 49.3%].

2-Bromo-3-methylindole: Yield: 2.57 g, 81% as a white solid, mp 88°C (lit.[28] mp 88-90°C), which could be stored in ethereal solution at -15°C. R_f 0.57 (hexane:diethyl ether 9:1). Found (M, $^{81}Br)^+$ 211.0852.

$C_9H_8N^{81}Br$ requires 211.0855; Found (M, $^{79}Br)^+$ 209.0869. $C_9H_8N^{79}Br$ requires 209.0875; ν_{max} (neat) 3391 (N–H), 786 & 735 (C–Br); δ_H (360 MHz; $CDCl_3$) 7.01-7.14 (3 H, m, C(5)**H**, C(6)**H** and C(7)**H**), 7.42 (1 H, d, 7.6, C(4)**H**), 7.96 (1 H, br s, N–**H**); δ_C (90.6MHz; $CDCl_3$) 9.9 (–CH_3), 110.1 (**C**(3)–Me), 112.1 (**C**(2)Br), 118.0 (**C**(6)H), 119.1 (**C**(4)H), 121.5 (**C**(5)H), 127.8 (**C**(3*a*)), 135.7 (**C**(7*a*)); *m/z* 211.1 [(M, $^{81}Br)^+$, 52%], 209.1 [(M, $^{79}Br)^+$, 49%], 130.1 [(M–Br)$^+$, 100%].

2-Bromo-5-methoxyindole: Yield: 3.47 g, 68% as a clear oil; R_f 0.35 (hexane:ethyl acetate 9:1). The product was unstable, decomposing to a dark green solid after several hours at room temperature, but could be stored in solution, in diethyl ether, at -20°C in the dark. Found (M, $^{81}Br)^+$ 227.0841. $C_9H_8N^{81}Br$ requires 227.0849; Found (M, $^{79}Br)^+$ 225.0858. $C_9H_8N^{79}Br$ requires 225.0869; ν_{max} (neat) 796 & 733 (C–Br); δ_H (360 MHz; $CDCl_3$) 3.77 (3 H, s, OCH_3), 6.38 (1 H, s, C(3)**H**), 6.79 (1 H, dd, *J* 8.8 and 2.4, C(6)**H**), 6.95 (1 H, d *J* 2.4, C(4)**H**), 7.03 (1 H, d, *J* 8.8, C(7)**H**), 8.65 (1 H, br s, N–**H**); δ_C (90.6MHz; $CDCl_3$) 55.8 (OCH_3), 101.6 (**C**(3)H), 104.4 (**C**(7)H), 109.2 (**C**(2)Br), 111.4 (**C**(6)H), 112.2 (**C**(4)H), 129.2 (**C**(3*a*)), 131.8 (**C**(7*a*)), 154.3 (**C**(5)OMe); *m/z* 227.1 [(M, $^{81}Br)^+$, 97.5%], 225.1 [(M, $^{79}Br)^+$, 100%], 146.1 [(M–Br)$^+$, 52%].

General Preparation of N-alkenyl-2-bromoindoles: (illustrated for N-(But-3'-ene)-2-bromoindole (1)):

Potassium carbonate (1.58 g, 11.46 mmol) was added to a solution of 2-bromoindole (0.75 g, 3.82 mmol) in acetone (25 ml) and heated to reflux. 4-Bromobut-1-ene (0.77 ml, 7.64 mmol) was added to the reaction mixture and the suspension stirred under reflux for 12 hr. After this time, a further amount of potassium carbonate (1.05 g, 7.64 mmol) and 4-bromobut-1-ene (0.77 ml, 7.64 mmol) was added and the mixture continued to be heated under reflux until tlc showed complete consumption of the 2-bromoindole - a further 12 hr. After cooling, the solvent was removed under reduced pressure and the residue taken up in water (100 ml), extracted with diethyl ether (2×100 ml) and the organic layer washed with water (2×50 ml), dried (magnesium sulphate) and concentrated. The product was purified by flash chromatography (hexane:ethyl acetate 9:1) to yield the *title compound* (103, 0.78 g, 81%) as a yellow oil; R_f 0.98 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 251.0062. $C_{12}H_{12}N^{81}Br$ requires 251.0134; Found (M, $^{79}Br)^+$ 249.0160. $C_{12}H_{12}N^{79}Br$ requires 249.0154; Found C–57.5, H–4.9, N–5.7. $C_{12}H_{12}NBr$ requires C–57.62, H–4.84, N–5.60. ν_{max} (neat) 1641 ($CH{=}CH_2$), 772 & 742 (C-Br); δ_H (360 MHz; $CDCl_3$) 2.46 (2 H, td, *J* 7.3, 7.2, C(2')$\mathbf{H_2}$), 4.17 (2 H, t, *J* 7.4, NC(1')$\mathbf{H_2}$), 5.06 (2 H, m, =C(4')$\mathbf{H_2}$), 5.77 (1 H, tdd, *J* 6.9, 10.1 and 13.8, C(3')**H**=), 6.54 (1 H, s, C(3)**H**), 7.14 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.50 (1 H, dd, *J* 6.2, 0.9, C(4)**H**); δ_C (90.6MHz; $CDCl_3$) 34.1 (**C**(2')H_2), 44.2 (N**C**(1')H_2), 104.0 (**C**(3)H), 109.5 (**C**(7)H), 112.8 (**C**(2)-Br), 117.5 (=**C**(4')H_2), 119.7 (**C**(6)H), 120.0 (**C**(4)H), 121.6 (**C**(5)H), 128.0 (**C**(3*a*)), 134.2 (**C**(3')H=), 136.2 (**C**(7*a*)); *m/z* 251.0 [(M, $^{81}Br)^+$, 63.6%], 249.0 [(M, $^{79}Br)^+$, 53.1%], 210.0 [(M, ^{81}Br–$CH_2CH{=}CH_2)^+$, 86.2%], 208.0 [(M, ^{79}Br–$CH_2CH{=}CH_2)^+$, 86.7%], 170.1 [(M–Br)$^+$, 100%].

N-(Pent-4'-ene)-2-bromoindole (2): Yield: 0.64 g, 64 % as a yellow oil; R_f 0.97 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 265.1283. $C_{13}H_{14}N^{81}Br$ requires 265.1771; Found (M, $^{79}Br)^+$ 263.1809. $C_{13}H_{14}N^{79}Br$ requires 263.1791; ν_{max} (neat) 1641 (C=C), 772 & 742 (C-Br); δ_H (360 MHz; $CDCl_3$) 1.86 (2 H, ddd, *J* 7.4 and 7.2, C(2')$\mathbf{H_2}$), 2.11 (2 H, ddd, *J* 6.2 and 7.2, C(3')$\mathbf{H_2}$), 4.15 (2 H, t, *J* 7.4, NC(1')$\mathbf{H_2}$), 5.04 (2 H, m, =C(5')$\mathbf{H_2}$), 5.81 (1 H, tdd, *J* 6.1, 10.2 and 16.8, C(4')**H**=), 6.55 (1 H, s, C(3)**H**), 7.16 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.51 (1 H, d, *J* 7.7, C(4)**H**); δ_C (90.6MHz; $CDCl_3$) 28.8 (**C**(2')H_2), 30.8 (**C**(3')H_2), 44.2 (N**C**(1')H_2), 104.0 (**C**(3)H), 109.5 (**C**(7)H), 112.9 (**C**(2)-Br), 115.5 (C=**C**(5')H_2), 119.7 (**C**(6)H), 120.0 (**C**(4)H), 121.6 (**C**(5)H), 128.1 (**C**(3*a*)), 136.3 (**C**(7*a*)), 137.3 (**C**(4')H=CH_2); *m/z* (EI)

265.0 [(M, $^{81}Br)^+$, 19.5%], 263.1 [(M, $^{79}Br)^+$, 18.6%], 224.0 [(M, $^{81}Br–CH_2CH=CH_2)^+$, 9.0%], 222.1 [(M, $^{79}Br–CH_2CH=CH_2)^+$, 8.0%], 184.0 [(M–Br)$^+$, 100%]; (CI) 264.0 [(M, ^{79}Br+H)$^+$, 100%], 266.0 [(M, ^{81}Br+H)$^+$, 94%].

N-(Hex-5'-ene)-2-bromoindole (3): Yield: 0.64 g, 64% as a yellow oil; R_f 0.97 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 279.0458. $C_{14}H_{16}N^{81}Br$ requires 279.0447; Found (M, $^{79}Br)^+$ 277.0468. $C_{14}H_{16}N^{79}Br$ requires 277.0467; ν_{max} (neat) 1639 (C=C), 771 & 744 (C-Br); δ_H (360 MHz; $CDCl_3$) 1.35 (2 H, ddd (appears as q), *J* 7.3, C(3')**H$_2$**), 1.67 (2 H, ddd (appears as q), *J* 7.4, C(4')**H$_2$**), 1.98 (2 H, dd, *J* 7.3, 7.0, C(2')**H$_2$**), 4.02 (2 H, t, *J* 7.3, NC(1')**H$_2$**), 4.93 (2 H, m, =C(6')**H$_2$**), 5.69 (1 H, tdd, *J* 6.7, 10.2 and 16.9, C(5')**H**=), 6.51 (1 H, s, C(3)**H**), 7.02-7.18 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.46 (1 H, d, *J* 7.7, C(4)**H**); δ_C (90.6MHz; $CDCl_3$) 25.8 (**C**(2' or 3')H_2), 29.1 (**C**(2' or 3')H_2), 33.2 (**C**(4')H_2), 44.4 (**NC**(1')H_2), 103.8 (**C**(3)H), 109.4 (**C**(7)H), 112.9 (**C**(2)Br), 114.8 (=**C**(6')H_2), 119.7 (**C**(6)H), 119.9 (**C**(4)H), 121.5 (**C**(5)H), 127.9 (**C**(3*a*)), 136.1 (**C**(7*a*)), 138.0 (**C**(5')H=); *m/z* 279.1 [(M, $^{81}Br)^+$, 25.8%], 277.0 [(M, $^{79}Br)^+$, 25.3%], 198.1 [M–Br)$^+$, 100%].

N-(4'-Methylpent-3'-ene)-2-bromoindole (4): Yield: 0.65 g, 83% as a yellow oil; R_f 0.96 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 279.2058. $C_{14}H_{16}N^{81}Br$ requires 279.2040; Found (M, $^{79}Br)^+$ 277.2041. $C_{14}H_{16}N^{79}Br$ requires 277.2060; ν_{max} (neat) 1723 (C=C), 772 & 741 (C-Br); δ_H (360 MHz; $CDCl_3$) 1.45 (3 H, s, one of C(5')**H$_3$**), 1.64 (3 H, s, one of C(5')**H$_3$**), 2.39 (2 H, q, *J* 7.5, C(2')**H$_2$**), 4.10 (2 H, t, *J* 7.5, N-C(1')**H$_2$**), 5.14 (1 H, t, *J* 7.5, C(3')$(Me)_2$), 6.53 (1 H, s, C(3)**H**), 7.02-7.28 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.49 (1 H, d, *J* 7.2, C(4)**H**); δ_C (90.6MHz; $CDCl_3$) 17.5 (**C**(5')H_3), 25.7 (**C**(5')H_3), 28.7 (**C**(2')H_2), 44.6 (**NC**(1')H_2), 103.9 (**C**(3)H), 109.5 (**C**(7)H), 113.0 (**C**(2)Br), 119.6 (**C**(3')H), 119.7 (**C**(6)H), 119.9 (**C**(4)H), 121.2 (**C**(5)H), 128.1 (**C**(3*a*)), 135.1 (**C**(7*a*)), 136.3 (**C**(4')CH_3); *m/z* (EI) 279.0 [(M, $^{81}Br)^+$, 19.5%], 277.0 [(M, $^{79}Br)^+$, 21.0%], 210.0 [(M, $^{81}Br–CH_2CH=C(CH_3)_2)^+$, 100.0%], 208.0 [(M, $^{79}Br–CH_2CH=C(CH_3)_2)^+$, 98.0%], 198.0 [(M–Br)$^+$, 85%], 129 [(M–Br–$CH_2CH=C(CH_3)_2)^+$, 86%]; (CI) 280 [(M, ^{81}Br+H)$^+$, 97%], 278 [(M, ^{79}Br+H), 100.0%].

N-(3'-Methylbut-3'-ene)-2-bromoindole (5): Yield: 0.78 g, 81% as a yellow oil; R_f 0.98 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 265.0303. $C_{13}H_{14}N^{81}Br$ requires 265.0290. Found (M, $^{79}Br)^+$ 263.0274. $C_{13}H_{14}N^{79}Br$ requires 263.0310. ν_{max} (neat) 1650 (C=C), 773 & 738 (C–Br); δ_H (360 MHz; $CDCl_3$) 1.75 (3 H, s, –**CH$_3$**), 2.34 (2 H, t, *J* 7.3, C(2')**H$_2$**), 4.25 (2 H, t, *J* 7.3, NC(1')**H$_2$**), 4.68 (2 H, d, ^2J 16.0, =**CH$_2$**), 6.52 (1 H, s, C(3)**H**), 7.12 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.51 (1 H, d, *J* 6.2, C(4)**H**); δ_C (90.6MHz; $CDCl_3$) 21.6 (–CH_3), 31.4 (**C**(2')H_2), 44.1 (**NC**(1')H_2), 104.2 (**C**(3)), 109.1 (**C**(7)), 112.5 (**C**(2)-Br), 114.4 (=**C**(4')H_2), 119.8 (**C**(6)), 120.2 (**C**(4)), 121.3 (**C**(5)), 128.3 (**C**(3*a*)), 135.8 (**C**(7*a*)), 140.2 (**C**(3')=); *m/z* (EI) 265.0 [(M, $^{81}Br)^+$, 94%], 263.0 [(M, $^{79}Br)^+$, 100%], 196.9 [(M, $^{81}Br–C_5H_9)^+$, 63%], 194.9 [(M, $^{79}Br–C_5H_9)^+$, 65%], 184.1 [(M–Br)$^+$, 57%].

N-(But-3'-yn)-2-bromoindole (6): Yield: 0.39 g, 61%) as an unstable dark yellow oil; R_f 0.90 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 249.1338. $C_{12}H_{10}N^{81}Br$ requires 249.1344; Found (M, $^{79}Br)^+$ 247.1369. $C_{12}H_{10}N^{79}Br$ requires 247.1364; ν_{max} (neat) 2173 (acetylene), 786 & 740 (C-Br); δ_H (360 MHz; $CDCl_3$) 2.08 (1 H, t, *J* 2.7, C(4')**H**), 2.59 (2 H, dt, *J* 2.7 and 7.0, C(2')**H**), 4.08 (2 H, t, *J* 7.1, NC(1')**H$_2$**), 6.53 (1 H, s, C(3)**H**), 7.08-7.31 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.51 (1 H, d, *J* 7.2, C(4)**H**); *m/z* (EI) 249.1 [(M, $^{81}Br)^+$, 12.5%], 247.1 [(M, $^{79}Br)^+$, 12.0%], 168.1 [(M–Br)$^+$, 85%]; (CI) 250 [(M, ^{81}Br+H)$^+$, 98%], 248 [(M, ^{79}Br+H), 100.0%].

1-Trimethylsilyl-4-bromobut-1-yne: *n*-Butyllithium (17.8 ml (1.6M solution), 28.6 mmol) was added dropwise to a stirred solution of 3-butyn-1-ol (1.07 ml, 1.00 g, 14.27 mmol) in THF (20 ml) at -78°C and the resultant solution stirred at -78°C for 2 hours. After this time, trimethylsilyl chloride (3.1 g, 3.63 ml, 28.6

mmol) was added and the solution allowed to warm to room temperature. Dilute hydrochloric acid (20 ml) was added and the reaction stirred at room temperature for a further 30 minutes. The reaction mixture was extracted with diethyl ether (200 ml), the ethereal layer washed with water (2¥100 ml), dried (magnesium sulphate) and concentrated under reduced pressure to give 4-(trimethylsilyl)-3-butyn-1-ol as a clear oil (1.97 g, 97%), without further purification. The reaction was repeated on several different scales, all with comparable yields. Found $(M)^+$ 142.0731. $C_7H_{14}OSi$ requires 142.0814; ν_{max} (neat) 2213; δ_H (360 MHz; $CDCl_3$) 0.16 (9H, s, 3×**CH_3**), 2.49 (2 H, t, *J* 6.7, C(2)**H_2**), 3.38 (1 H, s, -**OH**), 3.70 (2 H, t, *J* 6.7, C(1)**H_2**OH); δ_C (90.6MHz; $CDCl_3$) -0.13 (3×**CH_3**), 23.9 (**C**(2)H_2), 60.6 (**C**(1)H_2OH), 86.2 (**C**(4)TMS), 103.4 (**C**(3)); *m/z* 142.0 [$(M)^+$, 0.5%], 127.1 [$(M–CH_3)^+$, 49.1%], 83.0 [$(M)^+$, 100%], 73.1 [$(TMS)^+$, 32.5%].

To a stirred solution of triphenylphosphine (13.80 g, 0.053 mol) and carbon tetrabromide (17.48 g, 0.053 mol) in diethyl ether (60 ml) at room temperature was added 4-trimethylsilyl-3-butyn-1-ol (6.82 g, 0.048 mol) and stirring continued at room temperature for two days. The resulting yellow suspension was filtered, dried (magnesium sulphate) and the solvent removed *in vacuo*, to give a yellow oil which was purified by distillation (Kügelrohr, 87-89°C @ 1.5 mmHg) to give the *title compound* as a clear liquid (111, 9.47 g, 96.3%); ν_{max} (neat) 2217; δ_H (360 MHz; $CDCl_3$) 0.59 (9H, s, 3×**CH_3**), 3.20 (2 H, t, *J* 7.5, C(3)**H_2**), 3.85 (2 H, t, *J* 7.5, C(4)**H_2**Br); δ_C (90.6MHz; $CDCl_3$) -0.09 (3×CH_3), 24.2 (**C**(3)H_2), 60.9 (**C**(4)H_2Br), 87.0 (**C**(1)–TMS), 103.2 (**C**(2)); *m/z* (too volatile for high resolution mass spectrum); (EI) 206.0 [(M, $^{81}Br)^+$, 4.0%], 204.0 [(M, $^{79}Br)^+$, 4.0%], 163.0 [$(M+H_2, ^{81}Br–3CH_3)^+$, 34.0%], 161 [$(M+H_2, ^{79}Br–3CH_3)^+$, 33.5%], 127 [$(M–Br)^+$, 26.0%].

N-(But-3'-yn-4'-trimethylsilyl)-2-bromoindole (7): Yield: 0.096 g, 59% as an unstable yellow oil; R_f 0.90 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 321.3159. $C_{15}H_{18}NSi^{81}Br$ requires 321.3164. Found (M, $^{79}Br)^+$ 319.3180. $C_{15}H_{18}N^{79}Br$ requires 319.3185. ν_{max} (neat) 2223 (acetylene), 785 & 738 (C–Br); δ_H (360 MHz; $CDCl_3$) 0.09 (9 H, s, 3×**CH_3**), 3.16 (2 H, t, *J* 7.1, C(2')**H**), 4.13 (2 H, t, *J* 7.1, NC(1')**H_2**), 6.54 (1 H, s, C(3)**H**), 7.04-7.33 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.55 (1 H, d, *J* 7.2, C(4)**H**); *m/z* (EI) 321.3 [(M, $^{81}Br)^+$, 63%], 319.3 [(M, $^{79}Br)^+$, 64%], 240.3 [$(M–Br)^+$, 100%]; (CI) 322 [(M, ^{81}Br+H)$^+$, 94%], 320 [(M, ^{79}Br+H), 100.0%].

N-(But-3'-ene)-2-bromo-3-methylindole (8): Yield: 0.49 g, 79% as a yellow oil; R_f 0.70 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 265.0357. $C_{13}H_{14}N^{81}Br$ requires 265.0290; Found (M, $^{79}Br)^+$ 263.0331. $C_{13}H_{14}N^{79}Br$ requires 263.0310; ν_{max} (neat) 1641 (C=C), 784 & 730 (C–Br); δ_H (360 MHz; $CDCl_3$) 2.22 (3 H, s, C(3)–**CH_3**), 2.35 (2 H, td, *J* 7.3 and 7.2, C(2')**H_2**), 4.03 (2 H, t, *J* 7.4, NC(1')**H_2**), 4.98 (2 H, m, =C(4')**H_2**), 5.68 (1 H, tdd, *J* 6.9, 10.2 and 13.8, C(3')**H**=), 7.00-7.14 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.42 (1 H, d, *J* 7.6, C(4)**H**); δ_C (90.6MHz; $CDCl_3$) 9.8 (C(3)–CH_3), 34.1 (**C**(2')H_2), 44.1 (**NC**(1')H_2), 109.1 (**C**(7)H), 110.3 (**C**(3)–Me), 112.1 (**C**(2)–Br), 117.1 (=**C**(4')H_2), 118.2 (**C**(6)H), 119.3 (**C**(4)H), 121.6 (**C**(5)H), 127.8 (**C**(3*a*)), 134.3 (**C**(3')H=), 135.9 (**C**(7*a*)); *m/z* 265.0 [(M, $^{81}Br)^+$, 11.2%], 263.0 [(M, $^{79}Br)^+$, 10.1%], 184.1 [$(M–Br)^+$, 28.9%], 223.9 [(M, $^{81}Br–CH_2CH=CH_2)^+$, 18.3%], 221.9 [(M, $^{79}Br–CH_2CH=CH_2)^+$, 17.8%], 129.9 [$(M–Br–CH_2CH_2CH=CH_2)^+$, 22.7%].

N-(Pent-4'-ene)-2-bromo-3-methylindole (9): Yield: 0.48 g, 74% as a yellow oil; R_f 0.74 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 279.0473. $C_{14}H_{16}N^{81}Br$ requires 279.0447; Found (M, $^{79}Br)^+$ 277.0491. $C_{14}H_{16}N^{79}Br$ requires 277.0466; ν_{max} (neat) 1615 (C=C), 783 & 733 (C–Br); δ_H (360 MHz; $CDCl_3$) 1.72 (2 H, m, C(2')**H_2**), 1.98 (2 H, m, C(3')**H_2**), 2.24 (3 H, s, C(3)–**CH_3**), 3.96 (2 H, t, *J* 7.1, NC(1')**H_2**), 4.96 (2 H, m, =C(5')**H_2**), 5.66 (1 H, tdd, *J* 6.4, 10.1 and 12.7, C(4')**H**=), 6.98-7.14 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.42 (1 H, d, *J* 7.6, C(4)**H**); δ_C (90.6MHz; $CDCl_3$) 9.7 (C(3)–CH_3), 28.7 (**C**(2')H_2), 30.6 (**C**(3')H_2), 43.9 (N-**C**(1')H_2), 108.9 (**C**(7)H), 110.0 (**C**(3)–Me), 112.0 (**C**(2)–Br), 115.1

(=C(5')H_2), 118.0 (C(6)H), 119.1 (C(4)H), 121.4 (C(5)H), 127.6 (C(3*a*)), 135.8 (C(7*a*), 136.4 (C(4')H=); *m/z* 279.0 [(M, $^{81}Br)^+$, 34.0%], 277.1 [(M, $^{79}Br)^+$, 35.6%], 224.0 [(M, ^{81}Br–$CH_2CH_2CH{=}CH_2)^+$, 20.1%], 222.0 [(M, ^{79}Br–$CH_2CH_2CH{=}CH_2)^+$, 19.5%], 198.1 [(M–Br)$^+$, 100.0%].

N-(But-3'-ene)-2-bromo-5-methoxyindole (10): Yield: 0.51 g, 82% as a yellow oil; R_f 0.96 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 281.1759. $C_{13}H_{14}NO^{81}Br$ requires 281.1766; Found (M, $^{79}Br)^+$ 279.1779. $C_{13}H_{14}NO^{79}Br$ requires 279.1786; ν_{max} (neat) 1620 (C=C), 794 & 730 (C–Br); δ_H (360 MHz; $CDCl_3$) 2.42 (2 H, td, *J* 7.3, 7.3, C(2')**H_2**), 3.77 (3 H, s, **OCH_3**), 4.10 (2 H, t, *J* 7.3, NC(1')**H_2**), 5.01 (2 H, m, =C(4')**H_2**), 5.73 (1 H, tdd, *J* 6.8, 10.3 and 13.8, C(3')**H**=), 6.43 (1 H, s, C(3)**H**), 6.81 (1 H, dd, *J* 2.4 and 8.8, C(6)**H**), 6.94 (1 H, d, *J* 2.4, C(4)**H**), 7.10 (1 H, d, *J* 8.8, C(7)**H**); δ_C (90.6MHz; $CDCl_3$) 34.2 (**C**(2')H_2), 44.4 (**NC**(1')H_2), 55.7 (**OCH_3**), 101.6 (**C**(3)H), 103.6 (**C**(7)H), 110.2 (**C**(6)H), 111.7 (**C**(4)H), 112.8 (**C**(2)Br), 117.4 (=**C**(4')H_2), 128.3 (**C**(3*a*)), 131.5 (**C**(7*a*)), 134.2 (**C**(3')H=), 154.3 (**C**(5)OMe); *m/z* (EI) 281.0 [(M, $^{81}Br)^+$, 23.5%], 279.0 [(M, $^{79}Br)^+$, 20.5%], 240.0 [(M, ^{81}Br–$CH_2CH{=}CH_2)^+$, 80.0%], 238.0 [(M, ^{79}Br–$CH_2CH{=}CH_2)^+$, 79.0%], 200.0 [(M–Br)$^+$, 100%]; (CI) 282.0 [(M, ^{81}Br+H)$^+$, 98%], 280.0 [(M, ^{79}Br+H)$^+$, 100%].

N-(Pent-4'-ene)-2-bromo-5-methoxyindole (11): Yield: 0.76 g, 78% as a pale yellow oil; R_f 0.8 (hexane:ethyl acetate 9:1). Found (M, $^{81}Br)^+$ 295.2029. $C_{14}H_{16}NO^{81}Br$ requires 295.2034; Found (M, $^{79}Br)^+$ 293.2060. $C_{14}H_{16}NO^{79}Br$ requires 293.2054; ν_{max} (neat) 1615 (C=C), 797 & 730 (C–Br); δ_H (360 MHz; $CDCl_3$) 1.76 (2 H, m, C(2')**H_2**), 1.98 (2 H, m, C(3')**H_2**), 3.71 (5 H, s, **OCH_3**), 3.99 (2 H, t, *J* 7.3 NC(1')**H_2**), 4.91 (2 H, m, =C(5')**H_2**), 5.69 (1 H, tdd, *J* 6.4, 10.1 and 12.7, C(4')**H**=), 6.36 (1 H, s, C(3)**H**), 6.73 (1 H, dd, *J* 8.9 and 2.4, C(6)**H**), 6.87 (1 H, d, *J* 2.4, C(4)**H**), 7.04 (1 H, d, *J* 8.9, C(7)**H**); δ_C (90.6MHz; $CDCl_3$) 28.9 (**C**(2')H_2), 30.8 (**C**(3')H_2), 44.3 (**NC**(1')H_2), 55.7 (**OCH_3**), 101.5 (**C**(3)H), 103.6 (**C**(7)H), 110.2 (**C**(6)H), 111.7 (**C**(4)H), 112.9 (**C**(2)Br), 115.4 (=**C**(5')H_2), 128.3 (**C**(3*a*)), 131.5 (**C**(7*a*)), 137.3 (**C**(4')H=), 154.2 (**C**(5)OMe); *m/z* (EI) 295.0 [(M, $^{81}Br)^+$, 14.5%], 293.0 [(M, $^{79}Br)^+$, 14.0%], 214.0 [(M–Br)$^+$, 100%]; (CI) 296.0 [(M, ^{81}Br+H)$^+$, 97%], 294.0 [(M, ^{79}Br+H)$^+$, 100%].

General Radical Cyclisation Methodology (as illustrated for 2,3-Dihydro-1-methyl-1H-pyrrolo[1,2-a]indole (12)):

Tributyltin hydride (0.94 ml, 1.02 g, 3.5 mmol) was added to a solution of *N*-(but-3'-ene)-2-bromoindole (0.5 g, 2.92 mmol) in toluene (25 ml) and after being heated to 100°C under argon, AIBN (a few crystals, *ca.* 10 mg) was added and the mixture continued to be refluxed under argon for 12 hr. After cooling, the toluene was removed under reduced pressure and the residue taken up in diethyl ether (100 ml), which was washed with 20% aqueous ammonia solution (4×100 ml), water (100 ml), dried (magnesium sulphate) and solvent removed under reduced pressure. The crude product was purified by flash chromatography (hexane followed by hexane:ethyl acetate 9:1) to yield the *title compound* (118, 0.39 g, 79%) as a yellow oil. R_f 0.9 (hexane:ethyl acetate 9:1). Found (M)$^+$ 171.2403. $C_{12}H_{13}N$ requires 171.2419; Found C–84.0, H–7.6, N–8.2. $C_{12}H_{13}N$ requires C–84.17, H–7.65, N–8.18; ν_{max} (neat) 2958, 1458; δ_H (360 MHz; $CDCl_3$) 1.26 (3 H, d, *J* 6.9, –**CH_3**), 2.09 (1 H, m, one of C(2)**H_2**), 2.68 (1 H, m, C(1)**H**), 3.33 (1 H, m, one of C(2)**H_2**), 3.91 (1 H, m, one of C(3)**H_2**), 4.05 (1 H, m, one of C(3)**H_2**), 6.13 (1 H, s, C(9)**H**), 7.03-7.30 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.62 (1 H, d, *J* 7.7, C(8)**H**); δ_C (90.6MHz; $CDCl_3$) 19.4 (**CH_3**), 32.0 (**C**(1)H), 36.8 (**C**(2)H_2), 43.0 (**C**(3)H_2), 102.3 (**C**(9)H), 110.9 (**C**(5)H), 119.6 (**C**(6)H), 120.6 (**C**(8)H), 121.8 (**C**(7)H), 127.7 (**C**(8*a*)), 131.0 (**C**(9*a*)), 135.8 (**C**(4*a*)); *m/z* (EI)171.0 [(M)$^+$, 73.0%], 170.1 [(M–H)$^+$, 48.0%], 156 [(M–$CH_3)^+$, 82.5%]; (CI) 172.0 [(M+H)$^+$, 100%].

Cyclisation of N-(Pent-4'-ene)-2-bromoindole gave two products (entry 13):

6,7,8,9-Tetrahydro-9-methylpyrido[1,2-a]indole: R_f 0.9 (hexane:ethyl acetate 9:1). Found $(M)^+$ 185.1217. $C_{13}H_{15}N$ requires 185.1204; ν_{max} (neat) 2962, 1451; δ_H (360 MHz; $CDCl_3$) 1.41 (3 H, d, *J* 6.8, –**CH$_3$**), 2.49 (1 H, m, one of C(8)**H$_2$**), 2.88 (1 H, m, one of C(8)**H$_2$**), 3.01 (1 H, m, one of C(7)**H$_2$**), 3.77 (1 H, dt, *J* 5.2 and 11.3, one of C(7)**H$_2$**), 4.07 (2 H, m, NC(6)**H$_2$**), 6.52 (1 H, s, C(1)**H**), 7.04–7.36 (3 H, m, C(3)**H**, C(4)**H**, C(5)**H**), 7.57 (1 H, d, *J* 7.9, C(2)**H**), C(9)**H** signal too weak and obscurred by other signals; δ_C (90.6MHz; $CDCl_3$) 22.7 (–**C**H$_3$), 29.1 (**C**(7 or 8)H$_2$), 30.6 (**C**(9)H), 31.2 (**C**(7 or 8)H$_2$), 45.6 (N**C**(6)H$_2$), 99.2 (**C**(1)H), 109.9 (**C**(5)H), 119.7 (**C**(4)H), 120.6 (**C**(2)H), 121.3 (**C**(3)H), 128.4 (**C**(1*a*)), 132.6 (**C**(9*a*)), 136.0 (**C**(5*a*)); *m/z* 185.1 [$(M)^+$, 100%], 170.1 [$(M–Me)^+$, 43%]; (CI) 186.0 [$(M+H)^+$, 100%].

N-(Pent-4'-ene)indole: Found $(M)^+$ 185.1217. $C_{13}H_{15}N$ requires 185.1204; ν_{max} (neat) 1640 (C=C); δ_H (360 MHz; $CDCl_3$) 1.86 (2 H, m, C(2')**H$_2$**), 2.03 (2 H, m, C(3')**H$_2$**), 4.06 (2 H, t, *J* 6.9 NC(1')**H$_2$**), 5.06 (2 H, m, =C(5')**H$_2$**), 5.79 (1 H, tdd, *J* 6.1, 10.2 and 16.8, C(4')**H**=), 6.28 (1 H, d, *J* 8.6, C(3)**H**), 7.05–7.36 (4 H, m, C(2)**H**, C(5)**H**, C(6)**H** and C(7)**H**), 7.66 (1 H, d, *J* 7.9, C(4)**H**); δ_C (90.6MHz; $CDCl_3$) 28.3 (**C**(2')H$_2$), 30.8 (**C**(3')H$_2$), 44.3 (N**C**(1')H$_2$), 101.1 (**C**(3)H), 109.6 (**C**(7)H), 115.6 (=**C**(5')H$_2$), 119.8 (**C**(6)H), 120.1 (**C**(4)H), 121.4 (**C**(5)H), 126.2 (**C**(2)H), 128.0 (**C**(3*a*)), 136.4 (**C**(7*a*)), 137.5 (**C**(4')H=); *m/z* 185.1 [$(M)^+$, 100%], 116.1 [(M–pentene)$^+$, 27%].

2,3-Dihydro-1-(1-methylethyl)-1H-pyrrolo[1,2-a]indole (15): Yield: 0.35 g, 71 % as a pale yellow oil; R_f 0.98 (hexane:ethyl acetate 9:1). Found $(M)^+$ 199.2923. $C_{14}H_{17}N$ requires 199.2956; ν_{max} (neat) 2857, 1458; δ_H (360 MHz; $CDCl_3$) 0.96 (3 H, d, *J* 6.7, one of C(**CH$_3$**)$_2$), 0.98 (3 H, d, *J* 6.7, one of C(**CH$_3$**)$_2$), 1.92 (1 H, m, one of C(2)**H$_2$**), 2.24 (1 H, dsept, *J* 1.9 and 6.7, **CH**(CH$_3$)$_2$), 2.57 (1 H, m, one of C(2)**H$_2$**), 3.08 (1 H, ddd, *J* 1.0, 6.6 and 7.2, C(1)**H**), 3.83-4.06 (2 H, m, NC(3)**H$_2$**), 6.16 (1 H, s, C(9)**H**), 6.99-7.19 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.52 (1 H, d, *J* 6.7, C(8)**H**); δ_C (90.6MHz; $CDCl_3$) 20.2 (CH(**C**H$_3$)$_2$), 31.8 (**C**(2)H$_2$), 31.9 (**C**(1)H), 43.2 (N**C**(3)H$_2$), 44.4 (**C**HMe$_2$), 93.2 (**C**(9)H), 109.3 (**C**(5)H), 119.2 (**C**(6)H), 120.2 (**C**(8)H), 120.4 (**C**(7)H), 127.8 (**C**(8*a*)), 132.4 (**C**(9*a*)), 133.1 (C(4*a*)); *m/z* (EI) 199.0 [$(M)^+$, 26%], 156.0 [$(M–CH(Me)_2)^+$, 49%]; (CI) 201.0 [$(M+2H)^+$, 69%), 200.0 [$(M+H)^+$, 100%], 157.0 [(M–[CH(Me)$_2$]+H)$^+$, 37%].

2,3-Dihydro-1,1-dimethylpyrrolo[1,2-a]indole (16): Yield: 0.11 g, 73% as a yellow oil. R_f 0.9 (hexane:ethyl acetate 9:1). Found $(M)^+$ 185.2671. $C_{13}H_{15}N$ requires 185.2682; ν_{max} (neat) 2968, 1682; δ_H (360 MHz; $CDCl_3$) 1.51 (6 H, s, C(1)–(**CH$_3$**)$_2$), 2.44 (2 H, t, *J* 7.0, C(2)**H$_2$**), 3.98 (2 H, t, *J* 7.0, C(3)**H$_2$**), 6.14 (1 H, s, C(9)**H**), 7.00-7.24 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.57 (1 H, d, *J* 7.7, C(8)**H**); δ_C (90.6MHz; $CDCl_3$) 21.8 (2×**C**H$_3$), 35.8 (**C**(2)H$_2$), 43.0 (**C**(3)H$_2$), 102.3 (**C**(9)H), 109.3 (**C**(5)H), 119.9 (**C**(6)H), 120.5 (**C**(8)H), 121.4 (**C**(7)H), 128.0 (**C**(8*a*)), 132.7 (**C**(9*a*)), 137.2 (**C**(4*a*)); *m/z* (EI) 185.2 [$(M)^+$, 84%], 155.0 [$(M–(CH_3)_2)^+$, 37%]; (CI) 186.0 [$(M+H)^+$, 100%].

1,9-Dimethyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole (19): Yield: 0.23 g, 73% as a pale yellow oil; R_f 0.9 (hexane:ethyl acetate 9:1). Found $(M)^+$ 185.1204. $C_{13}H_{15}N$ requires 185.1204; ν_{max} (neat) 2885, 1457; δ_H (360 MHz; $CDCl_3$) 1.59 (3 H, d, *J* 7.0, C(1)–**CH$_3$**), 2.32 (1 H, m, one of C(2)**H$_2$**), 2.54 (3 H, s, C(9)–**CH$_3$**), 2.90 (1 H, m, C(1)**H**), 3.57 (1 H, m, one of C(2)**H$_2$**), 4.07 (1 H, m, one of NC(1)**H$_2$**), 4.22 (1 H, m, one of NC(1)**H$_2$**), 7.26-7.40 (3 H, m, C(5)**H**, C(6)**H**, C(7)**H**), 7.43 (1 H, d, *J* 7.1, C(8)**H**); δ_C (90.6MHz; $CDCl_3$) 8.3 (C(3)–**C**H$_3$), 19.1 (–**C**H$_3$), 31.3 (**C**(1)H), 36.8 (**C**(2)H$_2$), 42.4 (N**C**(3)H$_2$), 100.3 (**C**(9)–CH$_3$), 109.0 (**C**(5)H), 118.2 (**C**(6)H)), 120.0 (**C**(8)H)), 121.2 (**C**(7)H)), 131.9 (**C**(8*a*)), 133.1 (**C**(9*a*)), 144.9 (**C**(4*a*)); *m/z* 185.1 [$(M)^+$, 100.0%], 170.1 [$(M–CH_3)^+$, 73.7%].

Cyclisation of N-(Pent-4'-ene)-3-methyl-2-bromoindole gave two products (entry 20):
1,9-Dimethyl-6,7,8,9-tetrahydropyrido[1,2-a]indole: R_f 0.8 (hexane:ethyl acetate 9:1). Found $(M)^+$ 199.1332. $C_{14}H_{17}N$ requires 199.1361; δ_H (360 MHz; $CDCl_3$) 1.26 (3 H, d, *J* 7.1, C(9)–CH_3), 2.29 (3 H, s, C(1)–CH_3), 2.37 (1 H, m, one of C(8)H_2), 2.78 (1 H, m, one of C(8)H_2), 3.23 (1 H, m, one of C(7)H_2), 3.68 (1 H, dt, *J* 4.8 and 11.0, one of C(7)H_2), 3.98 (2 H, m, NC(6)H_2), 7.00-7.22 (3 H, m, C(3)H, C(4)H, C(5)H), 7.48 (1 H, d, *J* 7.8, C(2)H), C(9)H signal weak and obscurred by other signals; *m/z* 199.1 [$(M)^+$, 93.7%], 184.1 [$(M–CH_3)^+$, 27.5%].

N-Pent-4'-ene-3-methylindole: R_f 0.8 (hexane:ethyl acetate 9:1). Found $(M)^+$ 199.1394. $C_{14}H_{17}N$ requires 199.1361; δ_H (360 MHz; $CDCl_3$) 1.72 (2 H, m, C(2')H_2), 1.98 (2 H, m, C(3')H_2), 2.24 (3 H, s, C(3)–CH_3), 3.97 (2 H, t, *J* 7.1, N–C(1')H_2), 4.97 (2 H, m, =C(5')H_2), 5.73 (1 H, tdd, *J* 6.4, 10.1 and 12.7, C(4')H=), 6.98-7.14 (4 H, m, C(2)H, C(5)H, C(6)H, C(7)H), 7.42 (1 H, d, *J* 7.9, C(4)H); δ_C (90.6MHz; $CDCl_3$) 9.7 (C(3)–CH_3), 28.7 (C(2')H_2), 30.6 (C(3')H_2), 43.9 (NC(1')H_2), 108.9 (C(7)H), 110.0 (C(3)–Me), 112.0 (C(2)–Br), 115.1 (=C(5')H_2), 118.0 (C(6)H), 119.1 (C(4)H), 121.4 (C(5)H), 127.6 (C(3*a*)), 135.8 (C(7*a*), 136.4 (C(4')H=); *m/z* 199.1 [(M)+, 94%], 130.1 [(M–pentene)$^+$, 14%].
7-Methoxy-2,3-dihydro-1-methyl-1H-pyrrolo[1,2-a]indole (21): Yield: 0.26 g, 91% as a pale yellow oil; R_f 0.8 (hexane:ethyl acetate 9:1). Found $(M)^+$ 201.2662. $C_{13}H_{15}NO$ requires 201.2682; ν_{max} (neat) 2954, 1233, 1164; δ_H (360 MHz; $CDCl_3$) 1.32 (3 H, d, *J* 6.9, –CH_3), 2.05 (1 H, m, one of C(2)H_2), 2.65 (1 H, m, one of C(2)H_2), 3.30 (1 H, ddd, *J* 1.1, 6.9 and 7.4, C(1)H), 3.79 (3 H, s, –OCH_3), 3.89-4.05 (2 H, m, NC(3)H_2), 6.04 (1 H, s, C(9)H), 6.75 (1 H, dd, *J* 2.4 and 8.7, C(6)H), 7.01 (1 H, d, *J* 2.4, C(8)H), 7.06 (1 H, d, *J* 8.7, C(5)H); δ_C (90.6MHz; $CDCl_3$) 19.6 (-CH_3), 32.4 (C(1)H), 36.9 (C(2)H_2), 43.3 (C(3)H_2), 55.9 (OCH_3), 91.2 (C(9)H), 102.8 (C(5)H), 109.9 (C(6)H), 110.0 (C(8)H), 128.3 (C(8*a*)), 131.7 (C(9*a*)), 134.6 (C(4*a*)), 153.9 (C(7)OMe)); *m/z* (EI) 201 [$(M)^+$, 100%], 186 [$(M–Me)^+$, 93%]; (CI) 202 [$(M+H)^+$, 100%].

Cyclisation of N-(Pent-4'-ene)-5-methoxy-2-bromoindole gave two products (entry 22):
3-Methoxy-6,7,8,9-Tetrahydro-9-methylpyrido[1,2-a]indole: R_f 0.9 (hexane:ethyl acetate 9:1). Found $(M)^+$ 215.2963. $C_{14}H_{17}NO$ requires 215.2950; ν_{max} (neat) 2928, 1484, 1236; δ_H (360 MHz; $CDCl_3$) 1.19 (3 H, d, *J* 6.8, –CH_3), 2.28 (1 H, m, one of C(8)H_2), 2.73 (1 H, m, one of C(8)H_2), 2.89 (1 H, m, one of C(7)H_2), 3.53 (1 H, dt, *J* 4.9 and 11.4, one of C(7)H_2), 3.67 (3 H, s, –OCH_3), 3.83 (2 H, t, *J* 6.8, C(6)H_2), 6.21 (1 H, s, C(1)H), 6.70 (1 H, dd, *J* 8.9 and 2.4, C(4)H), 6.84 (1 H, d, *J* 2.5, C(2)H), 7.17 (1 H, d, *J* 8.9, C(5)H), C(9)H signal too weak and obscurred by other signals; *m/z* (EI) 215.0 [$(M)^+$, 100%], 200.0 [$(M–Me)^+$, 97%]; (CI) 216.0 [$(M+H)^+$, 100%].
N-(pent-4'-ene)-5-methoxyindole: R_f 0.9 (hexane:ethyl acetate 9:1). Found $(M)^+$ 215.2963. $C_{14}H_{17}NO$ requires 215.2950; ν_{max} (neat) 1617 (C=C); δ_H (360 MHz; $CDCl_3$) 1.78-1.90 (4 H, m, C(2')H_2 and C(3')H_2), 3.66 (3 H, s, –OCH_3), 3.91 (2 H, t, *J* 7.3 N-C(1')H_2), 4.87 (2 H, m, =C(5')H_2), 5.57 (1 H, tdd, *J* 6.4, 10.1 and 12.7, C(4')H=), 6.00 (1 H, d, *J* 8.9, C(3)H), 6.73 (1 H, dd, *J* 8.9 and 2.4, C(6)H), 6.83-6.92 (2 H, m, C(2)H and C(4)H), 7.08 (1 H, d, *J* 8.9, C(7)H); *m/z* (EI) 215.0 [$(M)^+$, 100%]; (CI) 216.0 [$(M+H)^+$, 100%].

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