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SYNTHESIS OF 1,2,3,4,5,7-HEXAHYDRO-6*H*-AZOCINO[4,3-*b*]INDOL-6-ONES AS INTERMEDIATES FOR THE SYNTHESIS OF APPARICINE

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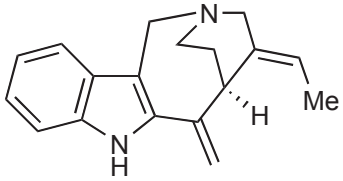
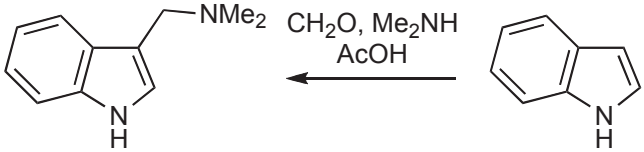
Abstract – 1-Phenylsulfonylindole is converted in eight steps into 2-(2-iodo-(*Z*)-but-2-en-1-yl)-6-methyl-1,2,3,4-tetrahydroazocino[4,3-*b*]indole, previously converted in one step into the indole alkaloid apparicine. The syntheses of other hexahydroazocino[4,3-*b*]indole potential precursors to the alkaloid are also described.

INTRODUCTION

The indole alkaloid apparicine emerged from Carl Djerassi's onslaught on the structures of alkaloids from South American *Aspidosperma* species; the paper[1] describing its structure determination was already XLVIII in his series 'Alkaloid Studies'. Apparicine, named for the Brazilian botanist Apparicio Duarte, and first isolated from *Aspidosperma dasycarpon*, was the first of what is now a substantially sized group of indole alkaloids[2] which lack one of the two ethanamine side-chain carbons of biosynthetic precursor tryptophan, having instead only one carbon between indole C-3 and the basic nitrogen, *i.e*. apparicine has a gramine unit and indeed the well-known reactivity of this moiety was utilized in the structural elucidation.[1]



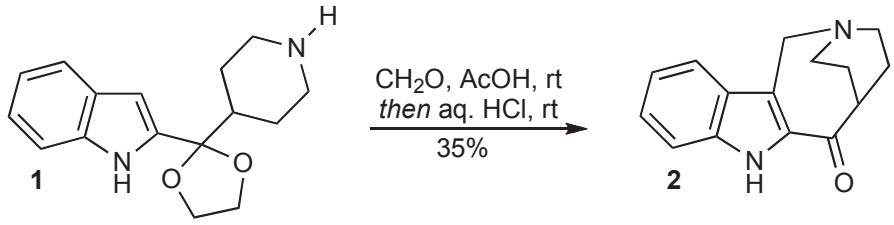
(–)-apparicine



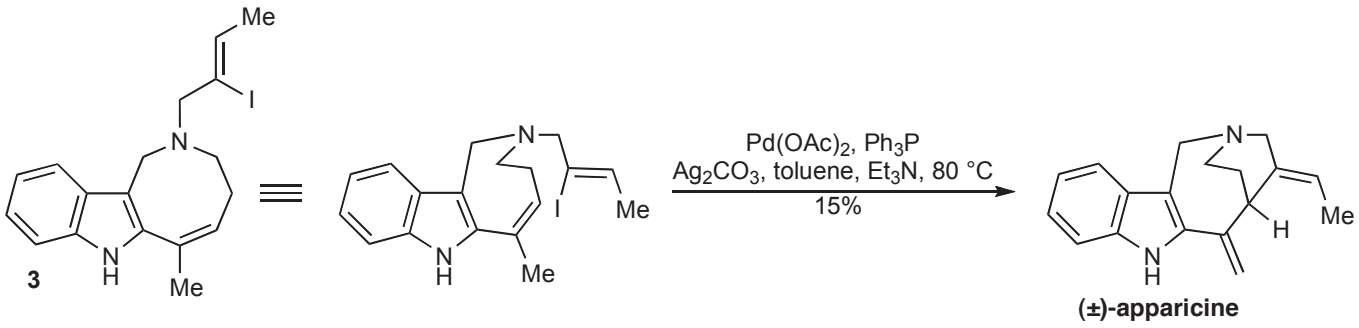
gramine

This paper is dedicated to Prof. Dr. Albert Eschenmoser on the occasion of his 85th birthday.

This structural parallelism prompted our first approach[3] to a synthesis of apparicine since it was known that gramine is formed easily from indole in a Mannich reaction: the piperidinyl-indolyl-ketal **1** was constructed *via* 2-acylation of the Grignard derivative of 4,5,6,7-tetrahydroindole (a pyrrole in reactivity terms), dehydrogenation to an indole, ketalisation, and reduction of the pyridine ring. Intramolecular Mannich reaction and hydrolysis of the acetal produced tetracycle **2** with the ring skeleton of apparicine.



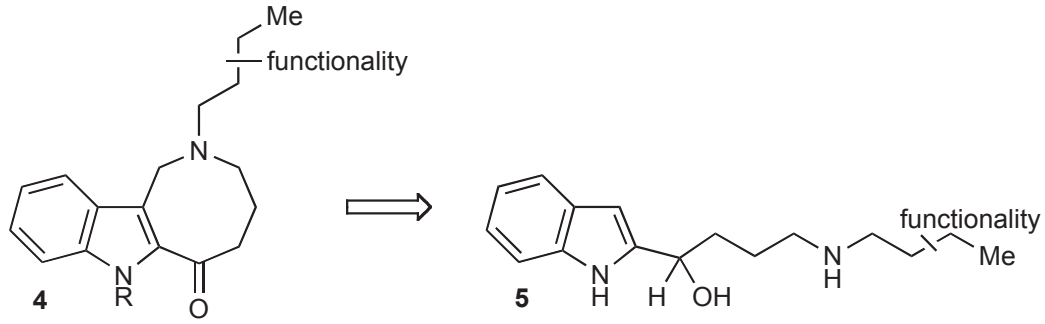
Our recent investigations relating to apparicine were not published since we were not able to complete the total synthesis, however, in 2009, Bennasar *et al*. described[4] the conversion (Scheme 1) of tricycle **3** into the alkaloid – this key intermediate was one of several with potential for forming the fourth, piperidine ring, that we had prepared. Our method of construction of this key intermediate and other similar compounds is now described in this paper; it is completely different to that of the Spanish group, which was based on ring-closing metathesis to form the eight-membered ring.



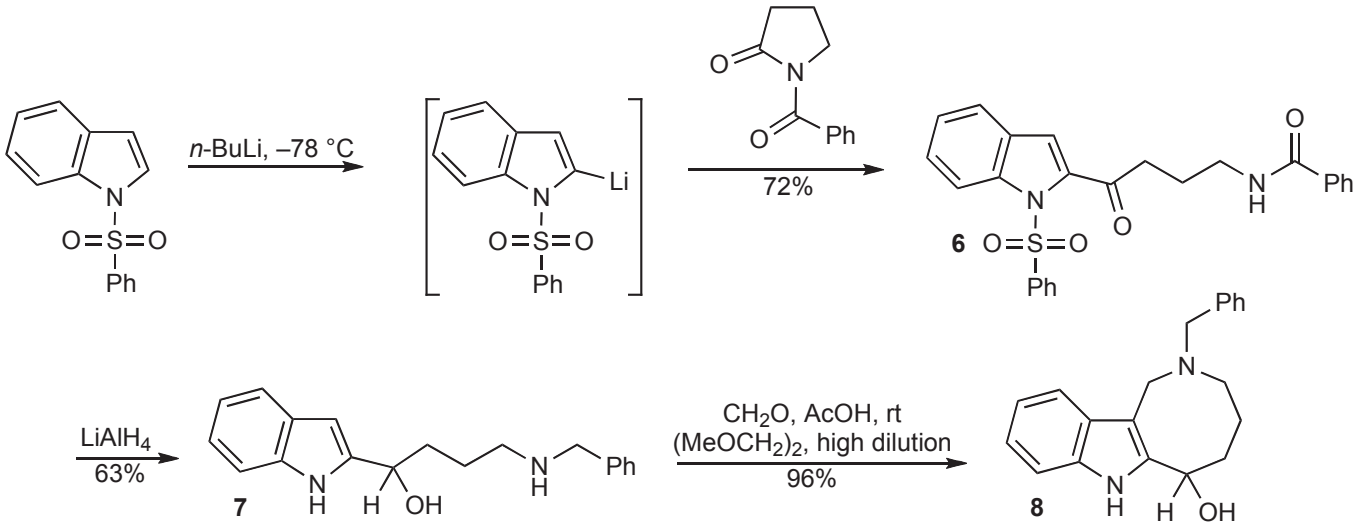
Scheme 1. Final step in the synthesis[4] of apparicine

RESULTS AND DISCUSSION

Since a ring-closing Mannich process had successfully produced tetracycle **2**, we determined to retain this reaction as a key element of a revised strategy in which the goal was to be a 1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-one of general form **4**. This would have a carbonyl for eventual conversion into exocyclic methylene and a functionalised *N*-substituent with potential for forming the piperidine ring, by a process that perhaps might also involve the ketone. This type of substance was to be formed *via* an intramolecular Mannich process but since this requires the absence of the deactivating carbonyl group, a precursor of the general form **5** was required.

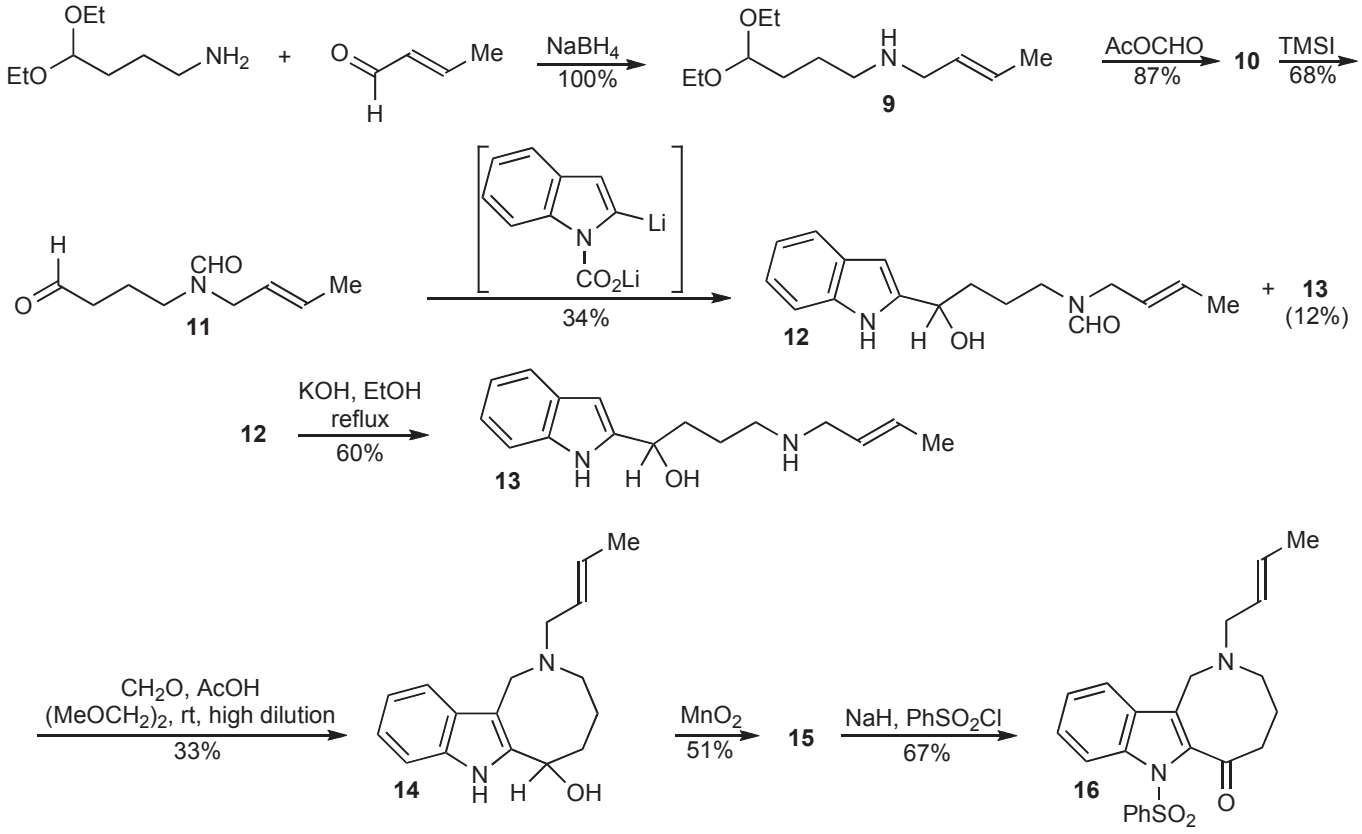


In earlier work,[5] 1-phenylsulfonylindole was lithiated at C-2[6] and thus reacted with the imide 1-benzoyl-2-pyrrolidone giving ketone **6**. Treatment with lithium aluminium hydride produced alcohol-amine **7** which closed very satisfactorily under high dilution conditions to **8**, thus establishing the viability of the approach (Scheme 2). However complications[7] arose on removal of the *N*-benzyl group and we sought a variation that would allow us the flexibility to introduce various functionalized *N*-side-chains to a tricyclic compound.

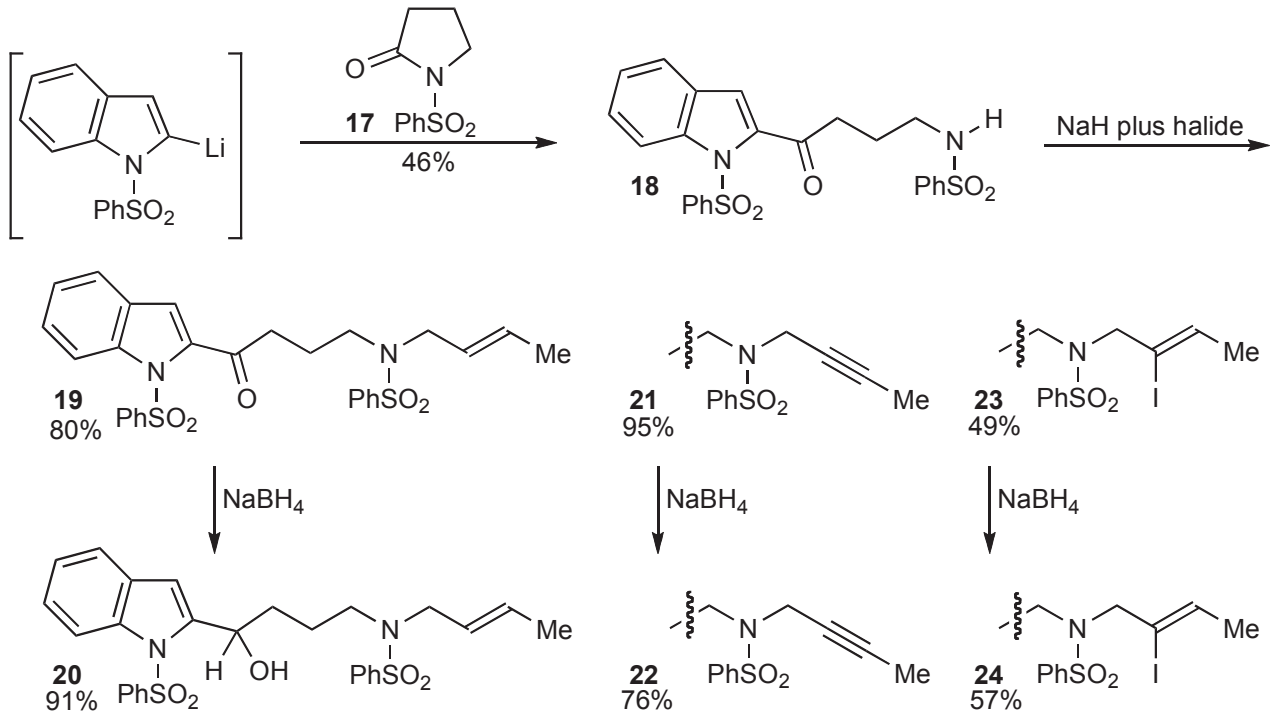


Scheme 2

In our first sequence, the whole of the indol-2-yl side-chain of the Mannich substrate was introduced at once. Reductive amination of crotonaldehyde with 4-aminobutanal diethyl acetal produced amine **9** which was *N*-formylated (→ **10**) before revealing the aldehyde function in **11** using iodotrimethylsilane. Reaction of the aldehyde with lithium 2-lithioindole-1-carboxylate[8] produced alcohol **12** requiring only formamide hydrolysis (→ **13**) before Mannich ring closure to **14**, manganese dioxide oxidation of the indolylic alcohol (→ **15**) and *N*-protection then producing the ketone **16**. An alternative route to alcohol **13** is described later.



Scheme 3

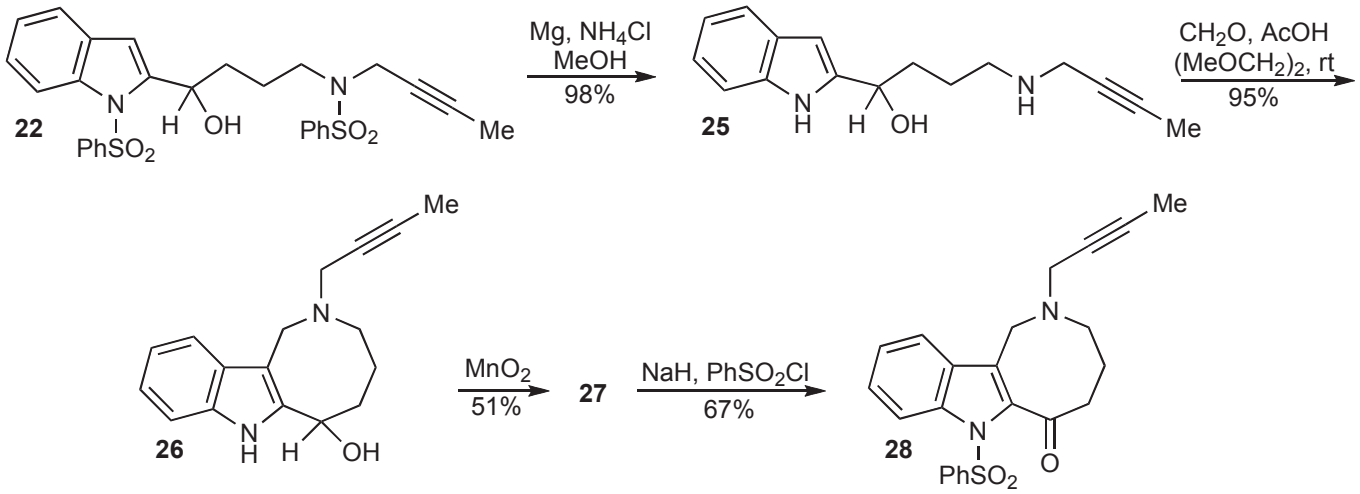


Scheme 4

This approach required a decision as to which *N*-side-chain to incorporate, at an early stage, so we developed an improvement that allows the side-chain unit to be introduced later in the sequence (Scheme

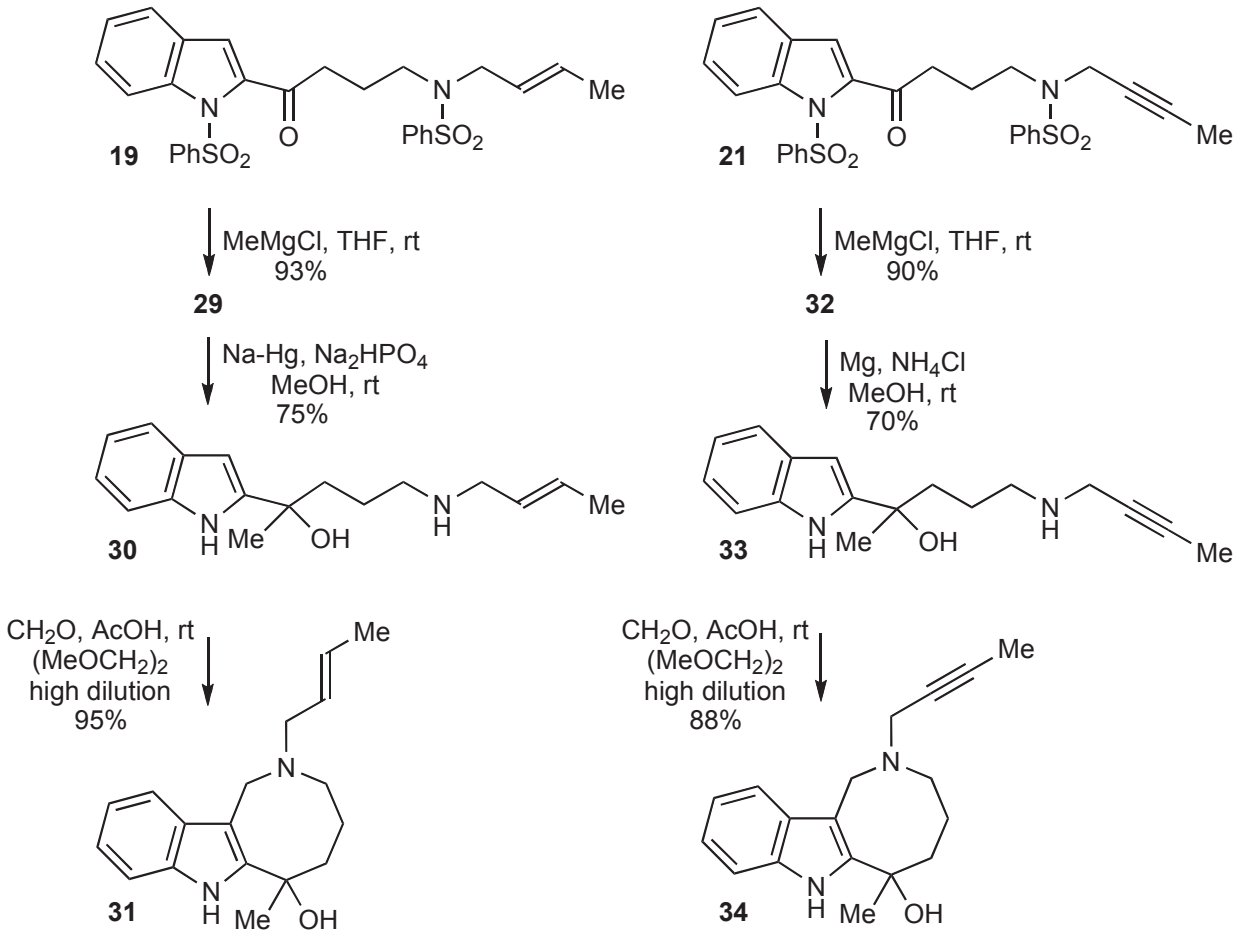
4). 2-Lithio-1-phenylsulfonylindole was reacted with 1-phenylsulfonyl-2-pyrrolidone **17** generating the key ketone **18**. This, with its acidic sulfonamide *N*-hydrogen, could be simply *N*-alkylated under mild conditions with a variety of halides, and thus were produced **19**, **21**, and **23**. Each of these was simply and efficiently reduced to the alcohol oxidation level (→ **20**, **22**, and **24**) that was to be needed for the Mannich ring closure.

The removal of phenylsulfonyl *N*-protection is not always easy and in these intermediates both an indole-*N*-phenylsulfonyl *and* an amine-*N*-phenylsulfonyl needed to be removed prior to Mannich cyclisation. Sodium amalgam proved relatively satisfactory (55%) for the conversion of **20** into the previously prepared butenyl-amine **13**. Mg-NH_4Cl in methanol[9] was an excellent choice for the conversion of **22** into amine **25** and Mannich closure of this gave the corresponding alkynyl-azocino-indole **26** in 95% yield, then oxidised (→ **27**) and *N*-protected forming ketone **28** (Scheme 5). Application of the Mg-NH_4Cl-MeOH method to iodo-butenyl alcohol **24** unfortunately removed the iodine as well as the phenylsulfonyl groups producing only butenyl-amine **13**, once again.



Scheme 5

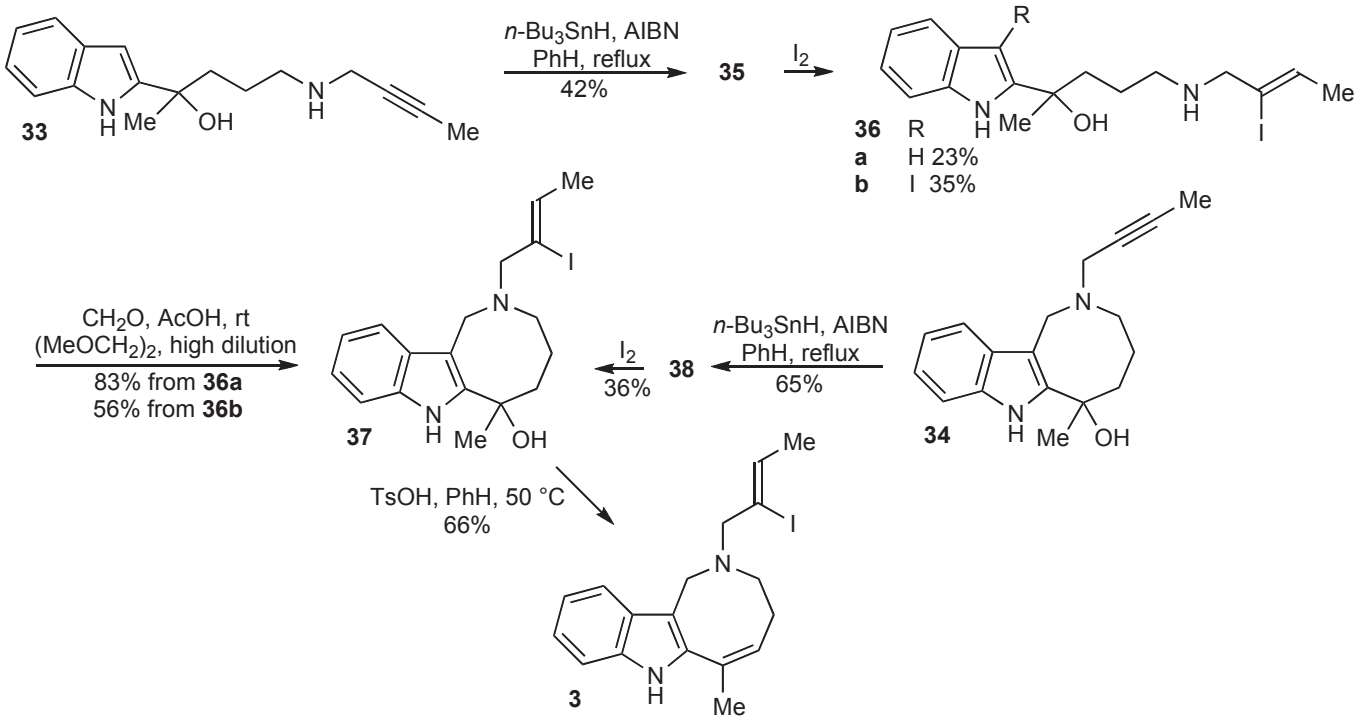
Our attention now turned to the missing carbon of the apparicine skeleton – that which is an exocyclic methylene in the alkaloid. Methyl Grignard addition to the still-protected ketones **19** and **21** proceeded unexceptionally (→ **29**, **32**), and after removal of the phenylsulfonyl groups, both of the resulting alcohols **30** and **33**, took part in Mannich ring closures very efficiently giving **31** and **34** respectively (Scheme 6).



Scheme 6

It remained to produce an azocino-indole with an iodo-butenyl side-chain (Scheme 7). To this end, we developed two variants: the alkynyl-alcohol **33** was hydrostannylated giving **35**. Although there are no examples of hydrostannation of propargylamines, we predicted the regiochemistry and stereochemistry of the hydrostannation based on analogy with the comparable reactions of propargylic alcohols, such as but-2-ynol, in which the tin attaches to C-2 giving a (*Z*)-vinylstannane.[10] Stannane **35** was then reacted with iodine, the *ipso* displacement of tin in a vinylstannane with iodine with retention of configuration being a well-recognised conversion.[10,11] This introduction of iodine was not a clean reaction in the sense that two products were formed, the desired **36a** and a product **36b** in which iodination at the indole 3-position had also taken place. Intriguingly, *both* of these underwent Mannich cyclisation to **37**. Dehydration of this alcohol produced **3**, the intermediate which, it was ultimately shown,[4] could be converted in one step into apparicine. The identity of this compound with that produced by the Spanish route also confirms the regio- and stereochemistry of the hydrostannation. Alternatively, the alkynyl-azocino-indole **34** could be hydrostannylated (→ **38**) then converted into iodide **37**.

In conclusion, we have described an efficient route to variously *N*-substituted 1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-ones, utilizing a high-dilution intramolecular Mannich reaction to form the eight-membered ring; one of these can be converted into apparicine in one step.[4] The precursors for the cyclisation were prepared *via* the use of 1-phenylsulfonyl-2-pyrrolidone in reaction with 2-lithio-1-phenylsulfonylindole: this, by selective reaction at the ring carbonyl then ring opening, generated an indol-2-yl 3-(phenylsulfonylamido)propyl ketone, the acidic *N*-hydrogen in which was then used for *N*-alkylations. This is the first time that 1-phenylsulfonyl-2-pyrrolidone has been used in this way and seems to offer an efficient general route to ketones of the type $R^1C(O)(CH_2)_3NHR^2$.



Scheme 7

EXPERIMENTAL

General

Flash column chromatography was performed using Merck Kieselgel 60 (230-400 mesh) silica. Tetrahydrofuran (THF) was dried by distillation from sodium-benzophenone; toluene (toluene) and dichloromethane were dried by distillation from calcium hydride; dimethylformamide was dried over 4 Å molecular sieves; organic extracts were dried over anhydrous $MgSO_4$. Solutions of *n*- and *t*-butyllithium and methylmagnesium chloride were purchased from the Aldrich chemical company and used without titration. UV spectra were recorded on a Shimadzu-260 UV-VIS recording spectrophotometer at fast scan speed, path length 1 cm in EtOH solution. IR spectra were recorded on a Perkin-Elmer 1710 Infra Red Fourier transform spectrometer as films. ^{1}H NMR spectra were recorded on a Varian AC 300E NMR

spectrometer operating at 300 MHz or a Varian Gemini 200 spectrometer operating at 200 MHz. Chemical shifts are reported in parts per million downfield from tetramethylsilane. Peak multiplicities are denoted by s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), quint (quintet) and m (multiplet) or by a combination of these *e.g*. dd (double doublet). ^{13}C NMR spectra were recorded on a Varian AC 300E NMR spectrometer at 75 MHz. Mass spectra were recorded on a Kratos MS 25 spectrometer. The modes of ionisation used are indicated as follows: electron impact (EI), chemical ionisation (CI) and fast atom bombardment (FAB). Accurate mass measurements were recorded on a Kratos concept. All reactions were carried out under a dry atmosphere of nitrogen or argon unless otherwise stated.

4-(*N*-(*E*-but-2-en-1-yl)amino)butanal diethyl acetal 9. 4-Aminobutanal diethyl acetal (10.0 mL, 11.6 mmol) and but-2-enal (10.0 mL, 24.4 mmol) were stirred in EtOH (150 mL) at 0 °C for 3 h. The reaction mixture was concentrated *in vacuo* then EtOH (100 mL) added. The solution was cooled to 0 °C and $NaBH_4$ (1.0 g, 23.3 mmol) added slowly. The mixture was allowed to come to rt and after 3 h, H_2O (50 mL) was added and the organic solvent evaporated. The product was extracted with Et_2O, the extract dried filtered and concentrated leaving the *amine* **9** as a yellow oil (12.4 g, 100%), showing a single spot on tlc (toluene:EtOAc, 1:1 plus 1% Et_3N) and used as such for the next step, ν_{max} 3312, 2974, 2931, 1673 cm^{-1}, δ_H ($CDCl_3$, 200 MHz) 5.53 (2H, m, NCH=CH), 4.46 (1H, t, *J* = 5 Hz, OCHO), 3.53 (4H, m, 2xOCH_2), 3.12 (2H, d, *J* = 5 Hz, NCH_2C=C), 2.57 (2H, m, CH_2CH_2N), 1.64 (3H, d, *J* = 5 Hz, CH_3C=C), 1.57 (4H, m, $CHCH_2CH_2$), 1.17 (6H, t, *J* = 6.5 Hz, 2xCH_3); *m/z* (CI) 216 (MH^+, 39%), 186 (9), 170 (17), 124 (19), 84 (20); $C_{12}H_{25}NO_2$ requires 215.1885. Found 215.1884.

4-(*N*-(*E*-but-2-en-1-yl)formamido)butanal diethyl acetal 10. To a stirred solution of acetic formic anhydride (1.4 g, 16.0 mmol) in dry THF (20 mL) at –70 °C was added 4-(*N*-(*E*-but-2-en-1-ylamino)butanal diethyl acetal **9** (2.87 g, 13.0 mmol) in THF (5 mL). The mixture was allowed to reach rt then stirred for 18 h. After concentration *in vacuo*, the residue was partitioned between Et_2O (20 mL) and H_2O (20 mL), the layers separated and the aqueous layer re-extracted with Et_2O (2x20 mL). The combined organic extracts were dried, filtered and evaporated leaving a red oil which was purified by chromatography over silica (toluene:EtOAc, 1:1) giving the *formamide* **10** as an orange oil (2.82 g, 87%), ν_{max} 2973, 1669 cm^{-1}; δ_H ($CDCl_3$, 200 MHz) 8.05 (1H, s, CH=O), 5.65 (1H, m, HC=C), 5.33 (1H, m, C=CH), 4.48 (1H, m, OCHO), 3.87 (1H, d, *J* = 6 Hz, one of NCH_2C=C), 3.75 (1H, d, *J* = 6 Hz, one of NCH_2C=C), 3.54 (4H, m, 2xCH_2CH_3), 3.25 (2H, m, CH_2CH_2N), 1.71 (2H, m, two of CH_2CH_2), 1.58 (11H, m, two of CH_2CH_2 plus 3xCH_3); *m/z* (FAB) 243 (M^+, 3%), 198 (100), 144 (15), 98 (40); $C_{13}H_{25}NO_3$ –C_2H_5OH requires 198.1480. Found 198.1494.

4-(*N*-(*E*-But-2-en-1-yl)formamido)butanal 11. To a stirred solution of 4-(*N*-(*E*-but-2-en-1-yl)-formamido)butanal diethyl acetal **10** (9.37 g, 39.0 mmol) in dry CH_2Cl_2 (100 mL) at rt was added iodotrimethylsilane (6.44 mL, 43.0 mmol) dropwise to give a deep red solution. Stirring was continued for 30 min, the reaction mixture washed with aq $Na_2S_2O_3$ (100 mL, 1M) and dried. Concentration gave an orange oil which was purified by chromatography over silica (toluene:EtOAc, 1:1) to give the *aldehyde* **11** as an orange oil (4.45 g, 68%), ν_{max} 2937, 1722, 1668 cm^{-1}; δ_H ($CDCl_3$, 200 MHz) 9.80 (1H, m, CH_2CH=O), 8.05 (1H, s, NCH=O), 5.66 (1H, m, HC=C), 5.36 (1H, m, C=CH), 3.85 (1H, d, *J* = 6 Hz, one of NCH_2C=C), 3.75 (1H, d, *J* = 6 Hz, one of NCH_2C=C), 3.27 (1H, t, *J* = 6 Hz, one of NCH_2CH_2), 3.24 (1H, t, *J* = 6 Hz, one of NCH_2CH_2), 2.50 (2H, m, CH_2C=O), 1.86 (2H, m, $CH_2CH_2CH_2$), 1.75 (3H, d, *J* = 6 Hz, CH_3); *m/z* (CI) 170 (MH^+, 100%); $C_9H_{15}NO_2$ requires 169.1103. Found 169.1104.

4-(*N*-(*E*-But-2-en-1-yl)formamido)-1-(indol-2-yl)butan-1-ol 12. To a stirred solution of indole (0.41 g, 3.5 mmol) in dry THF (10 mL) at –70 °C was added *n*-butyllithium (1.6 M solution in hexane, 2.39 mL, 3.8 mmol). The resulting suspension was held at –70 °C for 30 minutes, then CO_2 bubbled through to give a colourless solution, which was stirred for a further 10 min. The solvent was removed *in vacuo* (< 10 °C) to give a white crystalline solid that was redissolved in THF (10 mL). The solution was recooled to –70 °C and *t*-butyllithium (1.7 M solution in pentane, 5.77 mL, 3.8 mmol) added slowly to give a bright yellow solution which was stirred for 1 h at –70 °C. A solution of 4-(*N*-(*E*-but-2-en-1-yl)-formamido)butanal **11** (0.59 g, 3.5 mmol) in THF (5 mL) was added dropwise, the reaction mixture stirred for a further hour at –70 °C and subsequently allowed to warm to rt. The solution was poured into saturated aq NH_4Cl (30 mL), and extracted into Et_2O (2 x 20 mL). The combined organic extracts were dried and concentrated to give a brown oil which was purified by chromatography (EtOAc) to give the *alcohol* **12** as an orange oil (0.34 g, 34%), λ_{max} (log ε_{max}) 220 (4.14), 271 (3.75), 279 (3.74), 2.88 (3.63); ν_{max} 3298, 2934, 1654 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.82 (1H, bs, indol-1-yl-H), 8.00 (1H, s, CH=O), 7.56 (1H, d, *J* = 7.5 Hz, ArH), 7.38 (1H, d, *J* = 7.5 Hz, ArH), 7.15 (2H, m, ArH), 6.33 (1H, s, indol-3-yl-H), 5.62 (1H, m, HC=C), 5.36 (1H, m, C=CH), 4.92 (1H, t, *J* = 7 Hz, CHOH), 3.83 (1H, d, *J* = 7 Hz, one of NCH_2C=C), 3.66 (1H, d, *J* = 7 Hz, one of NCH_2C=C), 3.34 (1H, t, *J* = 7 Hz, one of NCH_2CH_2), 3.14 (1H, t, *J* = 7 Hz, one of NCH_2CH_2), 1.86 (2H, quint, *J* = 7 Hz, $CH_2CH_2CH_2$), 1.67 (5H, m+d, $NCH_2CH_2CH_2$ plus C=CCH_3); *m/z* (CI) 286 (M^+, 6%), 269 (78), 170 (53), 158 (23), 146 (27), 118 (60), 102 (48), 100 (61), 84 (33). Further elution (EtOH:Et_3N, 99:1) gave amine **13** (0.112 g, 12%) (see below for characterisation).

4-(*E*-But-2-en-1-ylamino)-1-(indol-2-yl)butan-1-ol 13. Method (a): 4-(*N*-(*E*-But-2-en-1-yl)formamido)-1-(indol-2-yl)butan-1-ol **12** (0.28 g, 1.0 mmol) and potassium hydroxide (1 g) were heated at reflux in

ethanol (15 mL) for 2 h. The reaction mixture was poured into water (50 mL) and product extracted into EtOAc (2 x 30 mL). The combined organic extracts were dried and concentrated to give a brown oil which was purified by chromatography (EtOH:Et_3N, 99:1) to give the *amine* **13** as waxy solid (0.15 g, 60%), λ_{max} (log ε_{max}) 218 (4.07), 271 (3.78), 280 (3.78), 288 (3.68); ν_{max} 3500, 3285, 2935 cm^{-1}; δ_H ($CDCl_3$, 200 MHz) 8.87 (1H, bs, indol-1-yl-H), 7.58 (1H, d, *J* = 7.5 Hz, ArH), 7.38 (1H, d, *J* = 7.5 Hz, ArH), 7.16 (1H, apparent t, *J* = 7.5 Hz, ArH), 7.10 (1H, apparent t, *J* = 7.5 Hz, ArH), 6.27 (1H, s, indol-3-yl-H), 5.61 (2H, m, HC=CH), 4.96 (1H, dd, *J* = 7.5, 2.3, Hz, C*H*OH), 4.22 (2H, bs, OH plus NH), 3.20 (2H, d, *J* = 7.5 Hz, NCH_2C=C), 2.76 (1H, m, one of NCH_2CH_2), 2.63 (1H, m, one of NCH_2CH_2), 2.18 (1H, m, one of $CH_2CH_2CH_2$), 2.03 (1H, m, one of $CH_2CH_2CH_2$), 1.88 (1H, m, one of $CH_2CH_2CH_2$), 1.74 (4H, d+m, one of $CH_2CH_2CH_2$ plus CH_3); *m/z* (CI) 259 (MH^+, 100%), 241 (80); $C_{16}H_{22}N_2O$ requires 258.1732. Found 258.1729.

Method (b): To a stirred solution of 4-(*N*-(*E*-but-2-en-1-yl)phenylsulfonylamido)-1-(1-phenylsulfonyl-indol-2-yl)butan-1-ol **20** (1.0 g, 1.9 mmol) and Na_2HPO_4 (2.6 g, 7.0 mmol) in dry MeOH (50 mL) at rt was added 6% sodium amalgam (10 g) gradually. Stirring was continued for 5 h, then the solution decanted from the residues, concentrated and partitioned between water (50 mL) and CH_2Cl_2 (50 mL). The aqueous layer was washed with CH_2Cl_2 (2 x 30 mL) and the combined organic extracts dried. Concentration gave a brown oil which was purified by chromatography (toluene:EtOAc:EtOH, 1:1:1) to give the *amine* **13** as a colourless waxy solid (0.266 g, 55%).

2-(*E*-But-2-en-1-yl)-1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-ol 14. Formalin (1.75 mL, 40%) and AcOH (1.75 mL) were added to a stirred solution of 4-(*E*-but-2-en-1-ylamino)-1-(indol-2-yl)butan-1-ol **13** (0.16 g, 0.6 mmol) in glyme (75 mL). After 30 min at rt the solution was concentrated *in vacuo* to ~3 mL then aq NaOH (10 mL, 3M) and Et_2O (10 mL) were added and the layers separated. The aqueous phase was extracted twice more with Et_2O, the combined extracts dried, filtered and evaporated leaving an oil (0.185 g) which was purified by chromatography over silica (toluene:EtOAc, 1:1 plus 1% Et_3N) giving the *tricycle* **14** as an orange oil (56 mg, 33%), λ_{max} (log ε_{max}) 223 (4.02), 274 (3.90), 281 (3.92), 289 (3.89); ν_{max} 3398, 3222, 2918, 2854 cm^{-1}; δ_H ($CDCl_3$+D_2O, 300 MHz) 7.54 (1H, d, *J* = 8.3 Hz, ArH), 7.35 (1H, d, *J* = 8.3 Hz, ArH), 7.20 (1H, t, *J* = 8.3 Hz, ArH), 7.13 (1H, t, *J* = 9 Hz, ArH), 5.70 (2H, m, CH=CH), 4.90 (1H, t, *J* = 3.8 Hz, CHO), 4.20 (1H, d, *J* = 15.8 Hz, one of $ArCH_2N$), 3.16 (1H, d, *J* = 15.6 Hz, one of $ArCH_2N$), 3.38 (1H, m, one of NCH_2C=C), 3.27 (1H, m, one of NCH_2C=C), 2.90 (1H, m, one of CH_2CH_2N), 2.59 (1H, m, one of CH_2CH_2N), 2.07 (1H, m, one of CH_2CH_2), 1.94 (2H, m, two of CH_2CH_2), 1.75 (4H, d+m, *J* = 7.5 Hz, one of CH_2CH_2 plus CH_3); *m/z* (CI) 271 (MH^+, 100%), 253 (38), 173 (33), 84 (30), 70 (25), 70 (25); $C_{17}H_{22}N_2O$ requires 270.1732. Found 270.1729.

2-(*E*-But-2-en-1-yl)-1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-one 15. To a stirred solution of 2-(*E*-but-2-en-1-yl)-1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-ol **14** (0.47 g, 1.7 mmol) in CH_2Cl_2 (100 mL) at rt was added MnO_2 (1.5 g). The resulting suspension was stirred for 72 h and then the solid filtered off and washed with CH_2Cl_2. Concentration of the solution gave a brown solid which was purified by chromatography (EtOAc:EtOH, 9:1). This gave the *ketone* **15** as a white crystalline solid (0.235 g, 51%), mp 139-141 °C, λ_{max} (log ε_{max}) 206 (4.26), 225 (3.98), 313 (4.12); ν_{max} 3329, 2918, 2812, 1629 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 9.10 (1H, bs, indol-1-yl-H), 7.67 (1H, d, *J* = 8.0 Hz, ArH), 7.40 (1H, d, *J* = 8 Hz, ArH), 7.38 (1H, t, *J* = 8 Hz, ArH), 7.19 (1H, t, *J* = 8.0 Hz, ArH), 5.54 (2H, bs, HC=CH), 4.45 (2H, bs, indol-3-ylCH_2N), 3.08 (4H, m, NCH_2C=C plus NCH_2CH_2), 2.65 (2H, m, CH_2C=O), 2.10 (2H, m, NCH_2CH_2CH_2), 1.71 (3H, d, *J* = 7.5 Hz, CH_3); *m/z* (EI) 268 (M^+, 100%), 213 (38), 185 (33), 170 (15), 157 (76), 143 (24), 129 (100), 110 (40), 84 (55); $C_{17}H_{20}N_2O$ requires C, 76.1; H, 7.5; N, 10.4%. Found C, 76.4; H, 7.6; N, 10.4%.

2-(*E*-But-2-en-1-yl)-1,2,3,4,5,7-hexahydro-7-phenylsulfonyl-6*H*-azocino[4,3-*b*]indol-6-one 16. To a stirred solution of 2-(*E*-but-2-en-1-yl)-1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-one **15** (0.88 g, 3.3 mmol) in dry DMF (50 mL) at rt was added NaH (60% dispersion in mineral oil, 0.144 g, 3.6 mmol). The solution was stirred until the evolution of H_2 had ceased (*ca*. 1 h), then $PhSO_2Cl$ (0.46 mL, 3.6 mmol) was added dropwise. Stirring continued for a further 1 h and then the reaction mixture was poured into water (100 mL) and product extracted into CH_2Cl_2 (2 x 40 mL). The combined organic extracts were dried and concentrated to give a brown oil which was purified by chromatography using (toluene:EtOAc, 99:1) to give *N-phenylsulfonyl-ketone* **16** as a yellow oil (0.9 g, 67%), λ_{max} (log ε_{max}) 220 (4.26); ν_{max} 2932, 1688 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.16 (2H, d, *J* = 8.0 Hz, ArH), 7.98 (1H, d, *J* = 8.0 Hz, indol-7-yl-H), 7.60-7.28 (6H, m, ArH), 5.50 (2H, m, HC=CH), 3.72 (2H, s, indol-3-ylCH_2N), 3.13 (2H, d, *J* = 5.5 Hz, NCH_2C=C), 2.74 (4H, m, CH_2CH_2CH_2), 2.00 (2H, m, CH_2CH_2CH_2), 1.65 (3H, d, *J* = 5.5 Hz, CH_3); *m/z* (CI) 409 (MH^+, 100%), 269 (36), 267 (40), 160 (23), 94 (31); $C_{23}H_{25}N_2O_3S$ requires 409.1586. Found 409.1577.

1-Phenylsulfonyl-2-pyrrolidone 17. Method (a). To a stirred solution of 2-pyrrolidone (20.0 g, 0.24 mol), *n*-Bu_4NHSO_4 (0.5 g, 1.5 mmol) and powdered NaOH (20.0 g, 0.5 mol) in dry CH_2Cl_2 (1 L) at 0 °C was added $PhSO_2Cl$ (33 mL, 45.3 g, 0.26 mol). The suspension was stirred for 18 h then poured into water (1 L). The organic layer was separated and the aqueous layer washed with CH_2Cl_2 (2 x 200 mL). The combined organic extracts were dried then concentration gave an orange oil which yielded the *sulfonamide* **17** as a white crystalline solid upon trituration with ethanol (11.90 g, 22%, mp 79-81 °C), ν_{max} 2985, 1739 cm^{-1}; δ_H ($CDCl_3$, 200 MHz) 8.02 (2H, d, *J* = 8 Hz, H-2',6'), 7.70-7.48 (3H, m, H-3',4',5'),

3.93 (2H, t, J = 8 Hz, NCH_2), 2.12 (2H, t, J = 8 Hz, $CH_2C{=}O$), 2.03 (2H, quint, J = 8 Hz, $CH_2CH_2CH_2$); m/z (EI) 226 (MH^+, 18%), 161 (100), 141 (20), 106 (72), 77 (90); $C_{10}H_{12}NO_3S$ requires 226.0538; Found 226.0529.

Method (b). To a stirred solution of 2-pyrrolidone (5 g, 6 mmol) in THF (150 mL) NaH (2.6 g, 60% dispersion in mineral oil, 6.6 mmol) was added carefully. The solution was stirred until the evolution of hydrogen had ceased (*ca*. 1 h), then $PhSO_2Cl$ (8.25 mL, 6.6 mmol) was added dropwise. Stirring was continued for a further 1 h then the reaction mixture was poured into water (200 mL) and product extracted into CH_2Cl_2 (2 x 100 mL). The combined organic extracts were dried and concentrated to give a brown oil which was purified by chromatography (toluene:EtOAc, 9:1) giving the *sulfonamide* **17** as white needles (5.42 g, 41%). All spectra as in Method (a).

4-Phenylsulfonylamido-1-(1-phenylsulfonylindol-2-yl)butan-1-one 18. To a stirred solution of 1-phenylsulfonylindole (20.0 g, 78.0 mmol) in dry THF (2 L) at –70 °C was added *n*-BuLi (1.6 M solution in hexane, 53.5 mL, 86.0 mmol) dropwise. The reaction mixture was allowed to rise to 0 °C over 30 min to give a deep orange solution which was then recooled to –70 °C. 1-Phenylsulfonyl-2-pyrrolidone **17** (17.5 g, 78.0 mmol) in THF (100 mL) was added dropwise and the solution allowed to rise to rt. Water (50 mL) was added and the reaction mixture concentrated *in vacuo* to *ca*. 50 mL. The solution was poured into saturated aq NH_4Cl (150 mL), and extracted into Et_2O (2 x 100 mL). The combined organic extracts were dried and concentrated to give a brown oil which was purified by chromatography using (toluene:EtOAc, 19:1→4:1) to give the *ketone* **18** as a pale brown crystalline solid (17.32 g, 46%), then triturated with EtOH, mp 111-113 °C; λ_{max} (log ε_{max}) 216 (5.26), 273 (5.11), 281 (5.11); ν_{max} 3291, 2936, 1690 cm^{-1}; δ_H ($CDCl_3$, 200 MHz) 8.14 (1H, d, J = 7.5 Hz, indol-7-yl-H), 7.92 (2H, d, J = 7.5 Hz, ArH) 7.60-7.20 (11H, m, ArH), 7.09 (1H, s, indol-3-yl-H), 4.82 (1H, bs, NH), 3.10 (4H, m, $CH_2CH_2CH_2$), 2.00 (2H, quint, J = 7.5 Hz, $CH_2CH_2CH_2$); δ_C ($CDCl_3$, 75 MHz) 194.1 (s), 139.9 (s), 139.3 (s), 138.5 (s), 137.9 (s), 134.0 (d), 132.6 (d), 129.1 (d), 129.0 (d), 128.5 (s), 127.6 (d), 127.3 (d), 127.0 (d), 124.5 (d), 123.0 (d), 117.0 (d), 115.6 (d), 42.4 (t), 39.1 (t), 24.1 (t); m/z (CI) 500 (MNH_4^+, 100%), 483 (MH^+, 4), 360 (87), 343 (38), 327 (36), 243 (53), 185 (42), 160 (71); $C_{24}H_{22}N_2O_5S_2 + NH_4$ requires 500.1314. Found 500.1311.

4-(*N*-(*E*-But-2-en-1-yl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)butan-1-one 19. To a stirred solution of 4-phenylsulfonylamido-1-(1-phenylsulfonylindol-2-yl)butan-1-one **18** (1.94 g, 4.0 mmol) in dry DMF (100 mL) at rt was added NaH (60% dispersion in mineral oil, 0.161 g, 4.0 mmol). The solution was stirred until the evolution of H_2 had ceased (*ca*. 1 h) then crotyl bromide (0.5 mL, 4.0 mmol) was added dropwise. Stirring continued for a further 1 h and then the reaction mixture was poured

into water (100 mL) and extracted into CH_2Cl_2 (2 x 40 mL). The combined organic extracts were dried and concentrated to give a brown oil which was purified by chromatography (toluene:EtOAc, 99:1) to give the *ketone* **19** as a white crystalline solid (1.72 g, 80%) mp 95-97 °C; λ_{max} (log ε_{max}) 207 (4.29), 273 (4.12), 281 (4.11); ν_{max} 2936, 1690 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.10 (1H, d, *J* = 7.5 Hz, indol-7-yl-H), 7.95 (2H, d, *J* = 7.5 Hz, ArH), 7.80 (2H, d, *J*=7.5 Hz, ArH), 7.60-7.27 (9H, m, ArH), 7.15 (1H, s, indol-3-yl-H), 5.61 (1H, m, HC=C), 5.23 (1H, m, C=CH), 3.79 (2H, d, *J* = 6.0 Hz, NCH_2C=C), 3.25 (2H, t, *J* = 6.0 Hz, NCH_2CH_2), 3.03 (2H, t, *J* = 6 Hz, CH_2C=O), 2.00 (2H, quint, *J* = 6 Hz, $CH_2CH_2CH_2$), 1.60 (3H, s, CH_3); *m/z* (CI) 554 (MNH_4^+, 100%), 537 (MH^+, 12%), 414 (37), 257 (17), 177 (38), 160 (44); $C_{28}H_{28}N_2O_5S_2$ requires C, 62.7; H, 5.2; N, 5.3; S, 11.9%. Found C, 62.9; H, 5.2; N, 5.3; S, 12.2%.

4-((*N*-But-2-ynyl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)butan-1-one 21. In a similar manner, 4-phenylsulfonylamido-1-(1-phenylsulfonylindol-2-yl)butan-1-one **18** (9.68 g, 20.0 mmol), NaH (60% dispersion in mineral oil, 0.8 g, 20.0 mmol) and bromobut-2-yne (2.57 g, 20.0 mmol) in DMF (500 mL) afforded a brown oil which was purified by chromatography (toluene:EtOAc, 99:1) to give *ketone* **21** as a white crystalline solid (10.72 g, 100%) mp 121-123 °C; λ_{max} (log ε_{max}) 217 (4.67), 285 (4.36); ν_{max} 3066, 2921, 1691 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.15 (1H, d, *J* = 7.5 Hz, indol-7-yl-H), 8.03 (2H, d, *J* = 7.5 Hz, ArH), 7.88 (2H, d, *J* = 7.5 Hz, ArH), 7.66-7.34 (9H, m, ArH), 7.18 (1H, s, indol-3-yl-H), 4.12 (2H, q, *J* = 1.5 Hz, $NCH_2C{\equiv}C$), 3.34 (2H, t, *J* = 7.5 Hz, NCH_2CH_2), 3.12 (2H, t, *J* = 7.5 Hz, CH_2C=O), 2.10 (2H, quint, *J* = 7.5 Hz, $CH_2CH_2CH_2$), 1.58 (3H, t, *J* = 1.5 Hz, CH_3); δ_C ($CDCl_3$, 75 MHz) 194.0 (s), 139.4 (s), 138.9 (s), 138.6 (s), 138.3 (s), 133.8 (d), 132.6 (d), 120.1 (s), 128.9 (s), 128.7 (s), 128.5 (d), 127.8 (d), 127.5 (d), 127.4 (d), 124.4 (d), 122.9 (d), 116.8 (d), 115.5 (d), 81.9 (s), 71.5 (s), 45.6 (t), 39.1 (t), 36.9 (t), 21.8 (t), 3.3 (q); *m/z* (CI) 535 (MH^+, 40%), 395 (42), 160 (100); $C_{28}H_{27}N_2O_5S_2$ requires 535.1361. Found 535.1366.

4-(*N*-(2-Iodo-*Z*-but-2-en-1-yl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)butan-1-one 23. In a similar manner, 4-phenylsulfonylamido-1-(1-phenylsulfonylindol-2-yl)butan-1-one **18** (12.0 g, 25.0 mmol), NaH (60% dispersion in mineral oil, 1.0 g, 27.0 mmol) and 1-bromo-2-iodo-*Z*-but-2-ene (6.5 g, 25.0 mmol) in DMF (500 mL) afforded a brown oil which was purified using chromatography (toluene:EtOAc, 99:1) to give the *ketone* **23** as a white crystalline solid (8.0 g, 49%) mp 131-132 °C, λ_{max} (log ε_{max}) 219 (5.03), 271 (4.56), 284 (4.57); ν_{max} 3063, 2928, 2875, 1690 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.15 (1H, d, *J* = 7.5 Hz, indol-7-yl-H), 8.00 (2H, d, *J* = 7.5 Hz, ArH), 7.86 (2H, d, *J* = 7.5 Hz, ArH), 7.64-7.31 (9H, m, ArH), 7.14 (1H, s, indol-3-yl-H), 5.96 (1H, q, *J* = 6.8 Hz, C=CH), 4.15 (2H, s, NCH_2C=C), 3.33 (2H, t, *J* = 7.5 Hz, NCH_2CH_2), 3.04 (2H, t, *J* = 7.5 Hz, CH_2C=O), 2.02 (2H, quint, *J* = 7.5 Hz, $CH_2CH_2CH_2$), 1.76 (3H, d, *J* = 6.8 Hz, CH_3); *m/z* (CI) 680 (MNH_4^+, 18%), 497 (22), 177 (23), 160

(100); $C_{28}H_{27}IN_2O_5S_2$ + NH_4 requires 680.0750; Found 680.0781.

4-(*N*-(*E*-But-2-en-1-yl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)butan-1-ol 20. To a stirred solution of 4-(*N*-(*E*-but-2-en-1-yl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)butan-1-one **19** (0.115 g, 0.2 mmol) in absolute ethanol (10 mL) at rt was added sodium borohydride (20 mg, 0.4 mmol). The solution was stirred for 3 h, water (2 mL) added, and stirring continued for a further 2 h. The solvent was removed *in vacuo* and the residue partitioned between water (10 mL) and CH_2Cl_2 (10 mL). The aqueous phase was re-extracted with CH_2Cl_2 (2 x 20 mL) and the combined organic extracts dried. Concentration gave an orange oil which was purified by chromatography (toluene: EtOAc, 85: 15) to give the *alcohol* **20** as a colourless oil (0.105 g, 91%), λ_{max} (log ε_{max}) 204 (4.74), 255 (4.60); ν_{max} 3509, 2921 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.15 (1H, d, *J* = 7.5 Hz, indol-7-yl-H), 7.81 (4H, m, ArH), 7.58-7.17 (9H, m, ArH), 6.69 (1H, s, indol-3-yl-H), 5.60 (1H, m, HC=C), 5.22 (2H, m, C=CH plus C*H*OH), 3.78 (2H, d, *J* = 6 Hz, NCH_2C=C), 3.23 (2H, t, *J* = 7 Hz, NCH_2CH_2), 2.05-1.70 (4H, m, $NCH_2CH_2CH_2$), 1.60 (3H, d, *J* = 6 Hz, CH_3); *m/z* (CI) 538 (M^+, 6%), 521 (27), 399 (47), 160 (100); $C_{28}H_{30}N_2O_5S_2$ + NH_4 requires 556.1940. Found 556.1954.

4-(*N*-(But-2-ynyl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)butan-1-ol 22. In a similar manner, 4-([*N*-but-2-ynyl]phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)butan-1-one **21** (3.28 g, 6.1 mmol) and sodium borohydride (0.57 g, 14.0 mmol) in ethanol (200 mL) afforded a yellow oil which was purified by chromatography (toluene: EtOAc, 85: 15) to give the *alcohol* **22** as a white crystalline solid (2.49 g, 76%) mp 131.5-133 °C, λ_{max} (log ε_{max}) 210 (5.59), 244 (4.91); ν_{max} 3529, 3067, 2921, 2871, 2226 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.14 (1H, d, *J* = 7.5 Hz, indol-7-yl-H), 7.90 (2H, d, *J* = 7.5 Hz, ArH), 7.84 (2H, d, *J* = 7.5 Hz, ArH), 7.60-7.25 (9H, m, ArH), 6.73 (1H, s, indol-3-yl-H), 5.30 (1H, m, C*H*OH), 4.13 (2H, s, $NCH_2C{\equiv}C$), 3.37 (2H, m, NCH_2CH_2), 2.12 (2H, m, CH_2CHOH), 1.90 (2H, m, $CH_2CH_2CH_2$), 1.55 (3H, s, CH_3); *m/z* (CI) 554 (MNH_4^+, 2%), 536 (M^+, 1%), 519 (5), 239 (15), 160 (100), 118 (27); $C_{28}H_{28}N_2O_5S_2$ requires C, 62.7; H, 5.2; N, 5.2; S, 11.9%. Found C, 62.5; H, 5.3; N, 5.3; S, 12.2%.

4-(*N*-(2-Iodo-(*Z*)-but-2-en-1-yl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)butan-1-ol 24. In a similar manner, 4-(*N*-(2-Iodo-(*Z*-)-but-2-en-1-yl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)-butan-1-one **23** (8.0 g, 12.0 mmol) and sodium borohydride (1.0 g, 27.0 mmol) in ethanol (500 mL) afforded a yellow oil which was purified by chromatography (toluene: EtOAc, 85: 15) to give the *alcohol* **24** as a colourless oil (4.55 g, 57%), λ_{max} (log ε_{max}) 216 (5.18), 248 (4.70), 290sh (4.07); ν_{max} 3528, 2924 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.14 (1H, d, *J* = 7.5 Hz, indol-7-yl-H), 7.86 (2H, d, *J* = 7.5 Hz, ArH), 7.83 (2H, d, *J* = 7.5 Hz, ArH), 7.61-7.19 (9H, m, ArH), 6.70 (1H, s, indol-3-yl-H), 5.95 (1H, q, *J* = 7.5 Hz,

C=CH), 5.68 (1H, m, C*H*OH), 4.13 (2H, s, NCH_2C=C), 3.34 (2H, t, *J* = 7.5 Hz, NCH_2CH_2), 2.00 (2H, m, $NCH_2CH_2CH_2$), 1.78 (5H, d+m, $CH_2CH_2CH_2$ plus CH_3); *m/z* (CI) 664 (M^+, 30%), 647 (20), 497 (32), 469 (22), 371 (19), 355 (35), 160 (100); $C_{28}H_{29}IN_2O_5S_2$ + NH_4 requires 682.0892. Found 682.0892.

4-(But-2-ynylamino)-1-(indol-2-yl)butan-1-ol 25. Method A. To a stirred solution of 4-(*N*-(but-2-ynyl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)butan-1-ol **23** (0.42 g, 0.8 mmol), Na_2HPO_4 (0.433 g, 3.0 mmol) in dry MeOH (50 mL), 6% sodium amalgam (10 g) was added gradually. After 5 h stirring, the solution was decanted off, solvent evaporated and the residue partitioned between water (40 mL) and CH_2Cl_2 (40 mL). The dried organic extract was evaporated and the residue purified by chromatography giving the *alcohol* **25** as a white crystalline solid (0.158 g, 75%), mp 94-95 °C, λ_{max} (log ε_{max}) 218 (4.62), 265 (4.00), 280 (3.97), 288 (3.87); ν_{max} 3287, 2918, 2855 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.83 (1H, bs, indol-1-yl-H), 7.60 (1H, d, *J* = 7.5 Hz, ArH), 7.40 (1H, d, *J* = 7.5 Hz, ArH), 7.19 (1H, t, *J* = 7.5 Hz, ArH), 7.13 (1H, t, *J* = 7.5 Hz, ArH), 6.29 (1H, s, indol-3-yl-H), 4.98 (1H, m, C*H*OH), 4.19 (2H, bs, OH plus NH), 3.40 (2H, m, $NCH_2C{\equiv}C$), 2.90 (1H, m, one of NCH_2CH_2), 2.73 (1H, m, one of NCH_2CH_2), 2.17 (1H, m, one of $NCH_2CH_2CH_2$), 2.07 (1H, m, one of $NCH_2CH_2CH_2$), 1.88 (4H, m+s, one of $NCH_2CH_2CH_2$ plus CH_3), 1.75 (1H, m, one of $NCH_2CH_2CH_2$); *m/z* (CI) 257 (*M*H$^+$, 70%), 239 (100%). (MM 257.1654. $C_{16}H_{21}N_2O$ requires 257.1654).

Method B. A suspension of magnesium (10 g, 0.42 mol) and ammonium chloride (0.19 mol) in dry MeOH (500 mL) containing 4-(*N*-(but-2-ynyl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)-butan-1-ol **22** (5.41 g, 10.0 mmol) was vigourously stirred for 2 h, then water (100 mL) added and the reaction mixture concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (100 mL), washed with water (50 mL) and dried. Concentration gave a pale brown crystalline solid that was purified by chromatography to give the *alcohol* **25** as a white crystalline solid (2.63 g, 98%). All spectra were identical to those given above.

2-(But-2-ynyl)-1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-ol 26. To a stirred solution of 4-(but-2-ynylamino)-1-(indol-2-yl)butan-1-ol **25** (0.73 g, 2.9 mmol) in 1,2-dimethoxyethane (1 L) at rt was added formalin (8 mL, 40%) and AcOH (8 mL). After 30 min the solution was concentrated *in vacuo* to *ca*. 5 mL and aqueous NaOH (20 mL) and Et_2O (20 mL) were added. The aqueous phase was re-extracted with Et_2O (2 x 20 mL) and the combined organic extracts dried. Concentration gave a brown oil which was purified by chromatography (toluene:EtOAc:EtOH. 2:2:1). This gave the *azocino-indole* **26** as a colourless oil (0.76 g, 95%), λ_{max} (log ε_{max}) 223 (4.56), 274 (4.35), 288sh (4.24); ν_{max} 3396, 3225, 3056, 2918 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.28 (1H, bs, indol-1-yl-H), 7.51 (1H, d, *J* = 7.5 Hz, ArH), 7.35-7.12 (3H, m, ArH), 4.90 (1H, m, C*H*OH), 4.16 (1H, d, *J* = 15 Hz, one of indol-3-ylCH_2N), 3.90 (1H,

d, J = 15 Hz, one of indol-3-ylCH_2N), 3.60 (2H, m, NCH_2C≡C), 2.82 (2H, t, J = 6 Hz, NC$H_2$$CH_2$), 2.10-1.75 (4H, m, N$CH_2CH_2CH_2$), 1.90 (3H, t, J = 1.8 Hz, CH_3); *m/z* (CI) 269 (MH^+, 100%), 196 (12); $C_{17}H_{20}N_2O$ requires 268.1576; Found 268.1582.

2-(But-2-ynyl)-1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-one 27. A mixture of 2-(but-2-ynyl)-1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-ol **26** (0.77 g, 2.9 mmol) and manganese dioxide (2.5 g) was stirred in CH_2Cl_2 (50 mL) at rt for 72 h. Filtration and evaporation afforded a brown solid which was purified by chromatography (EtOAc). This gave the *ketone* **27** as a white crystalline solid (0.18 g, 23%), mp 162-163 °C, λ_{max} (log ε_{max}) 207 (4.36), 235sh (4.11), 312 (4.27); ν_{max} 3312, 2919, 2200, 1638 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 9.31 (1H, bs, indol-1-yl-H), 7.90 (1H, d, J = 8 Hz, ArH), 7.42 (2H, m, ArH), 7.22 (1H, t, J = 8 Hz, ArH), 4.63 (2H, s, indol-3-yl-CH_2N), 3.20 (2H, q, J = 1.6 Hz, NCH_2C≡C), 3.13 (2H, t, J = 8 Hz, NC$H_2$$CH_2$), 2.68 (2H, t, J = 8 Hz, CH_2C=O), 2.20 (2H, quint, J = 8 Hz, NCH_2C$H_2$$CH_2$), 1.90 (3H, t, J = 1.6 Hz, CH_3); *m/z* (CI) 267 (MH^+, 100%); $C_{17}H_{18}N_2O$ requires 266.1419. Found 266.1414.

2-(But-2-ynyl)-1,2,3,4,5,7-hexahydro-7-phenylsulfonyl-6*H*-azocino[4,3-*b*]indol-6-one 28. To a stirred solution of 2-(but-2-ynyl)-1,2,3,4,5,7-hexahydro-6*H*-azocino[4,3-*b*]indol-6-one **27** (0.155 g, 0.58 mmol) in dry DMF (10 mL), were added NaH (60% dispersion in mineral oil, 26 mg, 0.6 mmol) then, after H_2 evolution ceased, $PhSO_2Cl$ (0.081 mL, 0.6 mmol) dropwise. After 1 h the mixture was poured into water (50 mL) and poduct extracted into CH_2Cl_2. The dried extract was evaporated giving a brown oil which was purified by chromatography (toluene:EtOAc, 99:1) to give the *sulfonamido-ketone* **28** as a white crystalline solid (78 mg, 33%), mp 149-151 °C, λ_{max} (log ε_{max}) 206 (4.80), 246sh (4.37), 293sh (4.02); ν_{max} 2920, 2210, 1691 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.15 (2H, d, J = 7.5 Hz, ArH), 8.02 (1H, d, J = 7.5 Hz, indol-7-yl-H), 7.60-7.30 (6H, m, ArH), 3.87 (2H, s, indol-3-ylCH_2N), 3.40 (2H, s, NCH_2C≡C), 2.84 (4H, m, NC$H_2$$CH_2CH_2$), 2.02 (2H, m, N$CH_2CH_2$$CH_2$), 1.83 (3H, t, J = 1.5 Hz, CH_3); *m/z* (CI) 407 (MH^+, 100%), 267 (90); $C_{23}H_{23}N_2O_3S$ requires 407.1429. Found 407.1423.

5-(*N*-(*E*-But-2-en-1-yl)phenylsulfonylamido)-2-methyl-2-(1-phenylsulfonylindol-2-yl)pentan-2-ol 29. To a stirred solution of 4-(*N*-(*E*-but-2-en-1-yl)phenylsulfonylamido)-1-(1-phenylsulfonylindol-2-yl)-butan-1-one **19** (0.5 g, 0.9 mmol) in dry THF (50 mL) at rt was added MeMgCl (3 M solution in THF, 0.37 mL, 1.1 mmol) dropwise. The reaction mixture was heated at refluxed for 1 h, allowed to cool, then poured into water (100 mL). The aqueous phase was extracted with Et_2O (3 x 30 mL) and the combined organic extracts dried. Concentration gave a yellow oil which was purified by chromatography (toluene:EtOAc, 9:1) to give the *alcohol* **29** as a colourless oil (0.48 g, 93%), λ_{max} (log ε_{max}) 207 (4.51), 242sh (4.20), 291sh (3.60); ν_{max} 3530, 2939 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.04 (1H, d, J = 7.5 Hz,

indol-7-yl-H), 7.83 (4H, m, ArH), 7.62-7.16 (9H, m, ArH), 6.70 (1H, s, indol-3-yl-H), 5.50 (1H, m, HC=C), 5.20 (1H, m, C=CH), 4.95 (1H, bs, OH), 3.74 (2H, d, J = 7.5 Hz, NCH_2C=C), 3.18 (2H, m, NCH_2CH_2), 2.13 (2H, t, J = 7.5 Hz, CH_2CHOH), 1.77 (3H, s, CH_3), 1.60 (5H, d+m, C=CCH_3 plus $CH_2CH_2CH_2$); *m/z* (CI) 552 (M^+, 30%), 535 (74), 395 (92), 160 (100); $C_{29}H_{32}N_2O_5S_2$ + NH_4 requires 570.2096. Found 570.2110.

5-(*E*-But-2-en-1-ylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol 30. A mixture of 5-(*N*-[*E*-but-2-en-1-yl]-phenylsulfonylamido)-2-methyl-2-(1-phenylsulfonylindol-2-yl)pentan-2-ol **29** (0.42 g, 0.8 mmol), Na_2HPO_4 (0.433 g, 3 mmol) and 6% sodium amalgam (10 g) were stirred together in dry MeOH (50 mL) at rt. Decantation and evaporation followed by chromatography gave the *alcohol* **30** as a white crystalline solid (0.158 g, 75%), mp 78-80 °C), λ_{max} (log ε_{max}) 226 (4.61), 274 (4.68); ν_{max} 3285, 3056, 2922, 2853 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.95 (1H, bs, indol-1-yl-H), 7.60 (1H, d, J = 7.5 Hz, ArH), 7.49 (1H, d, J = 7.5 Hz, ArH), 7.14 (2H, m, ArH), 6.20 (1H, s, indol-3-yl-H), 5.60 (2H, m, HC=CH), 4.79 (2H, bs, OH plus NH), 3.17 (2H, d, J = 7 Hz, NCH_2C=C), 2.75 (1H, m, one of NCH_2CH_2), 2.63 (1H, m, one of NCH_2CH_2), 2.34 (1H, m, one of $NCH_2CH_2CH_2$), 2.00 (1H, m, one of $NCH_2CH_2CH_2$), 1.75 (5H, d+m, C=CCH_3 plus two of $NCH_2CH_2CH_2$), 1.63 (3H, s, CCH_3); *m/z* (CI) 273 (MH^+, 26%), 255 (100); $C_{17}H_{24}N_2O$ requires 272.1889. Found 272.1900.

2-(*E*-But-2-en-1-yl)-1,2,3,4,5,7-hexahydro-6*H*-6-methylazocino[4,3-*b*]indol-6-ol 31. 5-(*E*-But-2-en-1-ylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol **30** (0.117 g, 0.43 mmol), formalin (1.25 mL, 40%) and AcOH (1.25 mL) in 1,2-dimethoxyethane (100 mL) were stirred togegher at rt for 0.5 h. Concetration and extraction of product into Et_2O (2 x 20 mL) produced brown oil which was purified by chromatography (toluene:EtOH, 85:15). This gave the *azocino-indole* **31** as a white crystalline solid (0.122 g, 100%), mp 56-58 °C, λ_{max} (log ε_{max}) 230 (4.54), 284 (4.12); ν_{max} 3430, 3263, 2916, 2813 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 9.60 (1H, bs, indol-1-yl-H), 7.45 (1H, d, J = 7.5 Hz, ArH), 7.37 (1H, d, J = 7.5 Hz, ArH), 7.20 (1H, t, J = 7.5 Hz, ArH), 7.14 (1H, t, J = 7.5 Hz, ArH), 5.19 (2H, m, HC=CH), 4.26 (1H, d, J = 15 Hz, one of indol-3-ylCH_2N), 3.68 (1H, d, J = 15 Hz, one of indol-3-ylCH_2N), 3.39 (1H, m, one of NCH_2C=C), 3.25 (1H, m, one of NCH_2C=C), 3.00 (1H, t, J = 9 Hz, one of NCH_2CH_2), 2.58 (1H, t, J = 9 Hz, one of NCH_2CH_2), 2.02 (1H, t, J = 9 Hz, one of $NCH_2CH_2CH_2$), 1.83 (3H, s, CCH_3), 1.75 (3H, d, J = 7 Hz, C=CCH_3), 1.84-1.63 (3H, m, one of $NCH_2CH_2CH_2$ plus $NCH_2CH_2CH_2$); *m/z* (CI) 285 (MH^+, 100%), 267 (18); $C_{18}H_{24}N_2O$ requires 284.1889. Found 284.1888.

5-((*N*-But-2-ynyl)phenylsulfonylamido)-2-methyl-2-(1-phenylsulfonylindol-2-yl)pentan-2-ol 32. To a stirred solution of 4-((*N*-but-2-ynyl)phenylsulfonylamino)-1-(1-phenylsulfonylindol-2-yl)butan-1-one **21**

(5.77 g, 10.8 mmol) in dry tetrahydrofuran (200 mL) at rt was added methylmagnesium chloride (3 M solution in THF, 4.7 mL, 14.0 mmol) dropwise then the mixture was heated at reflux for 3 h. The reaction mixture was allowed to cool, then poured into water (500 mL). The aqueous phase was extracted with Et_2O (3 x 300 mL) and the combined organic extracts dried. Evaporation and chromatography (toluene:EtOAc, 9:1) gave the *alcohol* **32** as an orange oil (4.53 g, 76%), λ_{max} (log ε_{max}) 232 (4.55), 258 (4.68); ν_{max} 3531, 3300, 2939, 2280 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.04 (1H, d, *J* = 7.5 Hz, indol-7-yl-H), 7.87 (4H, m, ArH), 7.61-7.20 (9H, m, ArH), 6.74 (1H, s, indol-3-yl-H), 4.99 (1H, s, OH), 4.08 (2H, s, $NCH_2C{\equiv}C$), 3.25 (2H, t, *J* = 7.5 Hz, NCH_2CH_2), 2.21 (2H, m, $CH_2C(Me)(OH)$), 1.78 (3H, s, CH_3), 1.55 (5H, s+m, $CH_2C{\equiv}C$, $CH_2CH_2CH_2$); δ_C ($CDCl_3$, 75 MHz) 147.5 (s), 139.0 (s), 138.1 (s), 137.8 (s), 133.8 (d), 132.5 (d), 129.1 (d), 129.0 (s), 128.7 (d), 127.8 (d), 127.0 (d), 126.6 (d), 125.2 (d), 124.3 (d), 121.2 (d), 115.6 (d), 112.6 (d), 81.8 (s), 71.6 (s), 71.5 (s), 46.5 (t), 39.5 (t), 36.9 (t), 28.0 (q), 22.7 (t), 3.1 (q); *m/z* (CI) 550 (M^+, 23%), 533 (100%), 411 (30), 393 (60), 227 (43), 160 (50), 78 (42); $C_{29}H_{30}N_2O_5S_2$ + NH_4 requires 568.1940. Found 568.1946.

5-(But-2-ynylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol 33. A suspension of Mg (10.0 g, 0.42 mol) and NH_4Cl (0.19 mol) in dry MeOH (500 mL) containing 5-((*N*-but-2-ynyl)phenylsulfonylamino)-2-methyl-2-(1-phenylsulfonylindol-2-yl)butan-2-ol **32** (4.5 g, 8.0 mmol) was vigorously stirred for 2 h (Caution – exothermic), then water (100 mL) added and the reaction mixture concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (100 mL), washed with water (50 mL) and dried. Filtration and concentration gave a brown oil which was purified by chromatography (toluene:EtOAc:EtOH, 2:2:1) to give the *amine* **33** as an orange oil (1.14 g, 52%), λ_{max} (log ε_{max}) 222 (4.66), 271 (4.33), 279 (4.31), 286 (4.20); ν_{max} 3410, 3292, 2920 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.84 (1H, bs, indol-1-yl-H), 7.58 (1H, d, *J* = 7.5 Hz, ArH), 7.40 (1H, d, *J* = 7.5 Hz, ArH), 7.16 (1H, t, *J* = 7.5 Hz, ArH), 7.12 (1H, t, *J* = 7.5 Hz, ArH), 6.28 (1H, s, indol-3-yl-H), 3.55 (2H, bs, OH and NH), 3.32 (2H, s, $NCH_2C{\equiv}C$), 2.88 (1H, m, one of NCH_2CH_2), 2.51 (1H, m, one of NCH_2CH_2), 2.32 (1H, m, one of $NCH_2CH_2CH_2$), 2.00 (1H, m, one of $NCH_2CH_2CH_2$), 1.85 (3H, s, CH_3), 1.73 (2H, m, one of $NCH_2CH_2CH_2$), 1.60 (3H, s, CH_3); δ_C ($CDCl_3$, 75 MHz) 146.6 (s), 134.9 (s), 129.3 (s), 120.8 (d), 120.0 (d), 119.5 (d), 110.9 (d), 96.3 (d), 79.9 (s), 75.9 (s), 70.6 (s), 48.4 (t), 42.9 (t), 37.6 (t), 31.9 (q), 24.4 (t), 3.5 (q); *m/z* (CI) 271 (MH^+, 23%), 253 (100), 239 (25); $C_{17}H_{23}N_2O$ requires 271.1810. Found 271.1810.

2-(But-2-ynyl)-1,2,3,4,5,7-hexahydro-6*H*-6-methylazocino[4,3-*b*]indol-6-ol 34. To a stirred solution of 5-(but-2-ynylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol **33** (0.25 g, 0.9 mmol) in 1,2-dimethoxyethane (250 mL), formalin (3 mL, 40%) and AcOH (3 mL) were added at rt. The solution was concentrated *in vacuo* to *ca*. 5 mL and aqueous sodium hydroxide (10 mL) and Et_2O (20 mL) were added. The layers

were separated, the aqueous phase re-extracted (Et_2O, 2 x 20 mL) and the combined organic extracts dried. Evaporation after filtration gave a brown oil which was purified by chromatography (toluene:EtOH, 85:15). This gave the *azocino-indole* **34** as a white crystalline solid (0.23 g, 88%) mp 178-180 °C, λ_{max} (log ε_{max}) 230 (4.22), 284 (4.07), 292 (4.02); ν_{max} 3440, 3266, 2918 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 9.03 (1H, bs, indol-1-yl-H), 7.46 (1H, d, *J* = 7.5 Hz, ArH), 7.34 (1H, d, *J* = 7.5 Hz, ArH), 7.15 (2H, m, ArH), 4.20 (1H, d, *J* = 15 Hz, one of indol-3-yl-CH_2N), 3.89 (1H, d, *J* 15 Hz, one of indol-3-yl-CH_2N), 3.57 (1H, q, *J* = 1.6 Hz, one of $NCH_2C{\equiv}C$), 3.52 (1H, q, *J* = 1.6 Hz, one of $NCH_2C{\equiv}C$), 2.80 (2H, m, NCH_2CH_2), 2.02-1.63 (4H, m, $NCH_2CH_2CH_2$), 1.86 (3H, t, *J* = 1.6 Hz, $C{\equiv}CCH_3$), 1.74 (3H, s, CH_3); δ_C ($CDCl_3$, 75 MHz) 138.6 (s), 134.0 (s), 127.4 (s), 125.6 (d), 121.6 (d), 119.4 (d), 118.0 (d), 110.7 (s), 81.7 (s), 73.1 (s), 69.3 (s), 55.1 (t), 50.9 (t), 48.0 (t), 43.0 (t), 27.6 (q), 24.7 (t), 3.6 (q); *m/z* (CI) 282 (M^+, 20%), 265 (38), 249 (34), 229 (38), 182 (40), 173 (100), 152 (67); $C_{18}H_{22}N_2O$ requires 282.1732. Found 282.1730.

5-(2-Tri-*n*-butylstannyl-(*Z*)-but-2-en-1-ylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol 35. A solution of 5-(but-2-ynylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol **33** (0.613 g, 2.3 mmol), *n*-Bu_3SnH (6 mL, 7.7 mmol) and AIBN (0.1 g) in PhH (20 mL) was heated at reflux for 30 h. Concentration gave a yellow liquid which was filtered through a short column of silica to remove excess *n*-Bu_3SnH. The silica was extracted with MeOH and concentration of the extract gave a brown oil which was purified by chromatography (EtOAc) to give the *stannane* **35** as an orange oil (0.53 g, 42%), λ_{max} (log ε_{max}) 228 (4.28), 274 (4.05), 280 (4.06), 288 (3.96); ν_{max} 3301, 2956, 2925, 2853 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.66 (1H, bs, indol-1-yl-H), 7.55 (1H, d, *J*=7.5 Hz, ArH), 7.32 (1H, d, *J*=7.5 Hz, ArH), 7.10 (2H, m, ArH), 6.20 (2H, s+m, indol-3-yl-H plus C=CH), 3.21 (2H, s, $NCH_2C{=}C$), 2.67 (1H, m, one of NCH_2CH_2), 2.52 (1H, m, one of NCH_2CH_2), 2.26 (1H, m, one of $NCH_2CH_2CH_2$), 1.96 (1H, m, one of $NCH_2CH_2CH_2$), 1.75 (5H, d+m, *J*=7 Hz, $C{=}CCH_3$ plus two of $NCH_2CH_2CH_2$), 1.70-1.20 (18H, m, $Sn(CH_2CH_2CH_2)_3$, 1.55 (3H, s, CCH_3), 0.90 (9H, t, *J*=10 Hz, $3xCH_2CH_3$); *m/z* (EI) 563 (MH^+, 4%), 545 (5), 487 (100), 368 (20), 350 (20), 182 (49); (MM 487.2142. $C_{29}H_{50}N_2OSn - H_2O - C_4H_9$ requires 487.2135).

5-(*Z*-2-Iodobut-2-en-1-ylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol 36a and 5-(*Z*-2-Iodobut-2-en-1-ylamino)-2-methyl-2-(3-iodoindol-2-yl)pentan-2-ol 36b. Method (a). To a stirred solution of 5-(2-tri-*n*-butylstannyl-(*Z*)-but-2-en-1-ylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol **35** (0.1 g, 0.21 mmol) in CH_2Cl_2 (5 mL) at rt was added I_2 (52 mg, 0.21 mmol). The solution was stirred for 15 min then decolourised by washing with 1N aq $Na_2S_2O_3$ solution and dried. Concentration gave a purple oil which was purified by chromatography using (toluene:EtOH, 9:1) to give the *iodide* **36a** as a colourless oil (14 mg, 17%), λ_{max} (log ε_{max}) 228 (4.36), 276 (4.28), 288 (4.17); ν_{max} 3420, 3286, 2922, 2852 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.70 (1H, bs, indol-1-yl-H), 7.56 (1H, d, *J* = 7.5 Hz, ArH), 7.38 (1H, d, *J* = 7.5 Hz, ArH), 7.12

(2H, m, ArH), 6.19 (1H, s, indol-3-yl-H), 5.75 (2H, q, *J* = 7 Hz, C=CH), 3.36 (2H, s, NCH_2C=C), 2.73 (2H, bs, OH, NH), 2.63 (1H, m, one of NCH_2CH_2), 2.45 (1H, m, one of NCH_2CH_2), 2.32 (1H, m, one of $NCH_2CH_2CH_2$), 1.96 (1H, m, one of $NCH_2CH_2CH_2$), 1.75 (3H, d, *J* = 7 Hz, C=CCH_3), 1.73-1.52 (2H, m, two of $NCH_2CH_2CH_2$), 1.57 (3H, s, CCH_3); *m/z* (EI) 398 (M^+, 8%), 380 (22), 365 (80), 280 (30), 253 (75), 210 (50), 184 (55), 157 (100); $C_{17}H_{23}IN_2O$ requires 398.0855. Found 398.0862.

Method (b). In a similar manner, 5-(2-tri-*n*-butylstannyl-(*Z*)-but-2-en-1-ylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol **35** (0.53 g, 1.09 mmol) in CH_2Cl_2 (10 mL) and I_2 (1.38 g, 5.5 mmol) gave a purple oil from which product was obtained by chromatography (toluene:EtOH, 9:1) to give firstly *diiodide* **36b** as a colourless oil (0.2 g, 35%), λ_{max} (log ε_{max}) 230 (4.70), 278 (4.89); ν_{max} 3410, 3286, 2922, 2850 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 9.38 (1H, bs, indol-1-yl-H), 7.39 (2H, m, ArH), 7.18 (2H, t, *J* = 7.5 Hz, ArH), 5.81 (2H, q, *J* = 7 Hz, C=CH), 3.40 (2H, s, NCH_2C=C), 3.33 (1H, m, one of NCH_2CH_2), 3.27 (2H, bs, OH, NH), 3.02 (1H, m, one of NCH_2CH_2), 2.66 (1H, m, one of $NCH_2CH_2CH_2$), 1.86 (1H, m, one of $NCH_2CH_2CH_2$), 1.76 (3H, d, *J* = 7 Hz, C=CCH_3), 1.70 (2H, m, one of $NCH_2CH_2CH_2$), 1.62 (3H, s, CCH_3); *m/z* (EI) 525 (M^+, 50%), 399 (37), 381 (62), 316 (42), 253 (38), 160 (40). Next from the column was *iodide* **36a** as a colourless oil (0.1 g, 23%). All spectra were as above.

2-(2-Tri-*n*-butylstannyl-(*Z*)-but-2-en-1-yl)-1,2,3,4,5,7-hexahydro-6*H*-6-methylazocino[4,3-*b*]indol-6-ol 38. 2-(But-2-ynyl)-1,2,3,4,5,7-hexahydro-6*H*-6-methylazocino[4,3-*b*]indol-6-ol **34** (230 mg, 0.82 mmol) was dissolved in PhH and the solution degassed under nitrogen. Azobisisobutyronitrile (50 mg, 0.30 mmol) and tri-*n*-butyltin hydride (2 mL, 7.4 mmol) were added and the mixture heated at reflux for 3 h. Most of the solvent was removed *in vacuo* and the resulting solution filtered through a short pad of silica, eluting first with petroleum ether:Et_3N, 99:1, to remove excess tin hydride, and then with petroleum ether:EtOAc:Et_3N, 49.5:49.5:1 to give the *stannane* **38** as a yellow oil (310 mg, 65%), λ_{max} (log ε_{max}) 228 (4.56), 284 (3.89); ν_{max} 3272, 2954, 2924, 1460, 740 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 9.15 (1H, bs, indol-1-yl-H), 8.40 (1H, bs, OH), 7.50 (1H, m, ArH), 7.31 (1H, m, ArH), 7.17 (1H, m, ArH), 6.49 (1H, q, *J* = 6.4 Hz, C=CH), 4.37 (1H, d, *J* = 15.8 Hz, one of indol-3-ylCH_2N), 3.63 (1H, d, *J* = 15.8 Hz, one of indol-3-ylCH_2N), 3.49 (1H, d, *J*=14.2 Hz, one of NCH_2C=C), 3.32 (1H, d, *J* = 14.2 Hz, one of NCH_2C=C), 3.00 (1H, m, one of NCH_2CH_2), 2.55 (1H, m, one of NCH_2CH_2), 2.07 (1H, m, one of $NCH_2CH_2CH_2$), 1.95-1.35 (27H, m, 3x$SnCH_2CH_2CH_2$ plus one of $NCH_2CH_2CH_2$ plus C=CCH_3 plus CCH_3 plus $CH_2CH_2CH_2$), 0.98 (9H, t, *J* = 7.2 Hz, 3xCH_2CH_3); δ_C ($CDCl_3$, 75 MHz) 139.2 (s), 138.2 (d), 134.1 (s), 127.7 (s), 122.5 (s), 121.4 (d), 119.2 (d), 117.9 (d), 111.0 (d), 110.6 (s), 69.3 (s), 66.5 (t), 57.1 (t), 50.8 (t), 43.1 (t), 29.3 (t), 27.7 (q), 27.5 (t), 24.6 (t), 20.3 (q), 13.8 (q), 10.3 (t); *m/z* (CI) 575 (MH^+, 100%), 557 (62), 517 (10), 499 (20); $C_{26}H_{41}N_2O^{120}Sn$ (i.e. M-C_4H_9) requires 517.2240. Found 517.2223.

2-(2-Iodo-(*Z*)-but-2-en-1-yl)-1,2,3,4,5,7-hexahydro-6*H*-6-methylazocino[4,3-*b*]indol-6-ol 37. Method (a): 5-(2-Iodo-*Z*-but-2-en-1-ylamino)-2-methyl-2-(indol-2-yl)pentan-2-ol **36a** (0.1 g, 0.25 mmol), formalin (1 mL, 40%) and AcOH (1 mL) in 1,2-dimethoxyethane (100 mL) were stirred together for 30 min. Concentration *in vacuo* to *ca*. 5 mL, addition of aq NaOH (10 mL) and Et_2O (20 mL), separation of the layers, re-extraction of the aq layer, and finally drying of the organic solution and evaporation produced a brown oil which was purified by chromatography (toluene:EtOH, 85:15). This gave the *azocino-indole* **37** as a colourless oil (0.085 g, 83%), λ_{max} (log ε_{max}) 228 (4.77), 278 (4.87); ν_{max} 3420, 3264, 2917 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 9.62 (1H, bs, indol-1-yl-H), 7.41 (1H, d, *J* = 7.5 Hz, ArH), 7.35 (1H, d, *J* = 7.5 Hz, ArH), 7.19 (1H, t, *J* = 7.5 Hz, ArH), 7.14 (1H, t, *J* = 7.5 Hz, ArH), 5.94 (1H, q, *J* = 7 Hz, C=CH), 4.22 (1H, d, *J* = 15 Hz, one of indol-3-ylCH_2N), 3.76 (1H, d, *J* = 15 Hz, one of indol-3-ylCH_2N), 3.12 (2H, s, NCH_2C=C), 2.95 (1H, t, *J* = 9 Hz, one of NCH_2CH_2), 2.52 (1H, t, *J* = 9 Hz, one of NCH_2CH_2), 2.05 (1H, t, *J* = 9 Hz, one of $NCH_2CH_2CH_2$), 1.80 (3H, s, CCH_3), 1.75 (3H, d, *J* = 7 Hz, C=CCH_3), 1.84-1.65 (3H, m, three of $NCH_2CH_2CH_2$); δ_C ($CDCl_3$, 125 MHz) 138.7 (s), 134.8 (d), 133.8 (s), 127.4 (s), 121.6 (d), 119.3 (d), 117.7 (d), 110.9 (d), 110.3 (s), 104.5 (s), 71.9 (t), 69.2 (s), 56.7 (t), 50.9 (t), 42.9 (t), 27.6 (q), 24.6 (t), 22.1 (q); *m/z* (CI) 411 (MH^+, 100%), 393 (42), 316 (23), 269 (28), 211 (36); $C_{18}H_{23}IN_2O$ requires 410.0857. Found 410.0856.

Method (b): To a solution of 2-(2-tri-*n*-butylstannyl-(*Z*)-but-2-en-1-yl)-1,2,3,4,5,7-hexahydro-6*H*-6-methylazocino[4,3-*b*]indol-6-ol **38** (285 mg, 0.5 mmol) in CH_2Cl_2 (1 mL) was added I_2 (632 mg, 2.50 mmol) and the resulting mixture stirred at rt for 35 min, quenched with aq $Na_2S_2O_3$ and product extracted into CH_2Cl_2. Evaporation gave crude material which was purified by chromatography over silica (toluene:EtOAc, 95:5→9:1). Further partitioning between petroleum ether and MeCN gave highly pure product **37** (74 mg, 36%).

2-(2-Iodo-*Z*-but-2-en-1-yl)-1,2,3,4,-tetrahydro-6-methylazocino[4,3-*b*]indole 3. 2-(2-Iodo-(*Z*)-but-2-en-1-yl)-1,2,3,4,5,7-hexahydro-6*H*-6-methylazocino[4,3-*b*]indol-6-ol **37** (80 mg, 0.20 mmol) was dissolved in PhH with heating to 50 °C. *p*-toluenesulfonic acid (10 mg, 0.05 mmol) was added and the mixture heated at 50 °C for 30 min. The solvent was evaporated *in vacuo* and the residue partitioned between aq $NaHCO_3$ and CH_2Cl_2. The organic extract was dried and evaporated to give the *alkene* **3** as an oil (52 mg, 66%), λ_{max} (log ε_{max}) 234 (4.34), 296 (4.11); ν_{max} 3408, 2927, 2913, 1644 cm^{-1}; δ_H ($CDCl_3$, 300 MHz) 8.04 (1H, bs, indol-1-yl-H), 7.59 (1H, d, *J* = 7.5 Hz, ArH), 7.34 (1H, d, *J* = 7.5 Hz, ArH), 7.14 (2H, t, *J* = 7.5 Hz, ArH), 5.84 (2H, m, 2xC=CH), 4.00 (2H, s, indol-3-ylCH_2N), 3.37 (2H, s, NCH_2C=C), 2.72 (2H, m, NCH_2CH_2), 2.18 (5H, s+m, NCH_2CH_2 plus CCH_3), 1.80 (3H, d, *J* = 7 Hz, C=CCH_3); *m/z* (EI) 392 (M^+, 19%), 183 (55), 168 (60), 133 (41); $C_{18}H_{21}IN_2$ requires 392.0751. Found 392.0766.

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