

The tandem radical route to indole alkaloids: an unusual rearrangement reaction

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Abstract

Cyclisation of the precursor **6** under standard radical conditions yields the tetracyclic structure **7** which represents the core of a number of indole alkaloids along with the novel tetracycle **13**.

Keywords: Indoles, radical cyclisation, rearrangement, alkaloids

Introduction

The *Strychnos* and *Aspidosperma* alkaloids are structurally complex molecules that possess a range of biological activity and present a challenge to synthetic organic chemists.¹ As part of our ongoing interest in these classes of alkaloids,² we are particularly concerned with a synthesis of the core tetracyclic sub-structure **1**, which forms the basis of these molecules as exemplified by strychnine **2** and aspidospermidine **3** (Figure 1).

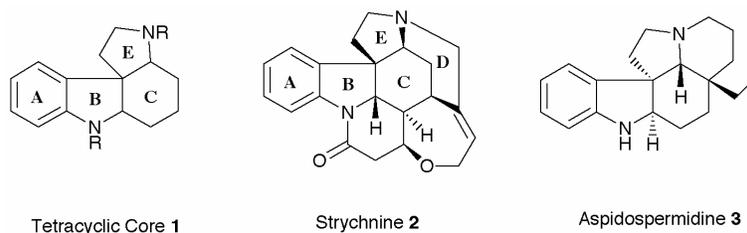
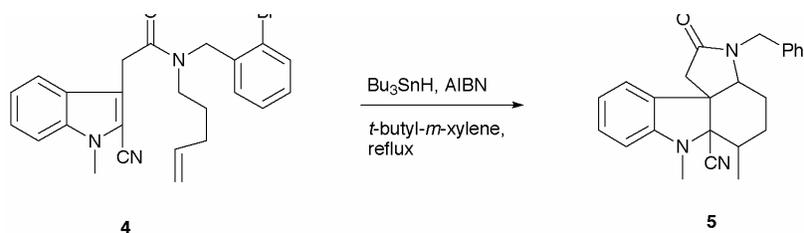


Figure 1

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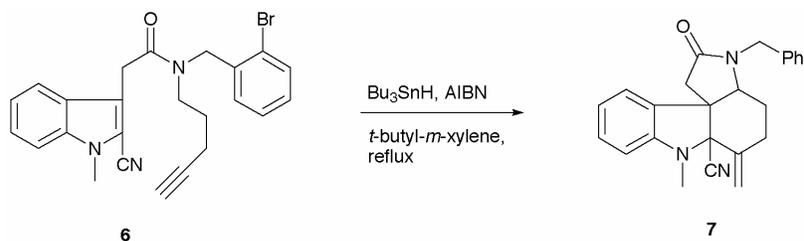
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In our previous studies, we had shown that tandem radical cyclisation of the precursor **4** gave the tetracyclic structure **5** as a mixture of 4 diastereoisomers (Scheme 1).³



Scheme 1

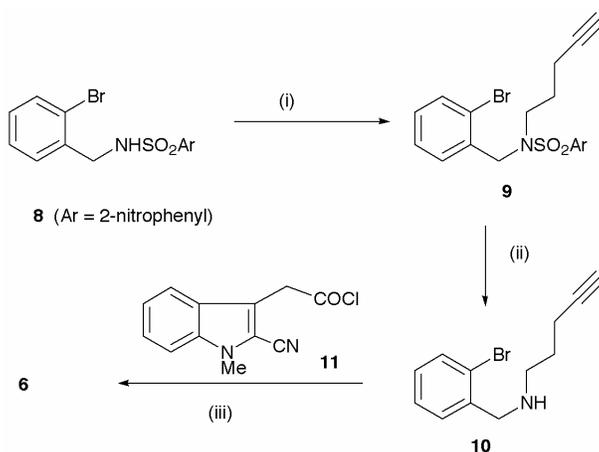
Whilst this route provided the core tetracyclic structure **5**, it possesses limited functionality with which to undertake a synthesis of either the *Strychnos* or *Aspidosperma* alkaloids. We therefore embarked on a synthesis of a cyclisation precursor which, after cyclisation, would enable us to access suitable intermediates for the synthesis of these two classes of alkaloids. The proposed cyclisation precursor **6** is shown below. It possesses a terminal C/C triple bond, which on cyclisation under our standard conditions should provide an exocyclic double bond on the tetracyclic product **7** (Scheme 2). This would allow further elaboration of such molecules towards natural products such as strychnine and aspidospermidine.



Scheme 2

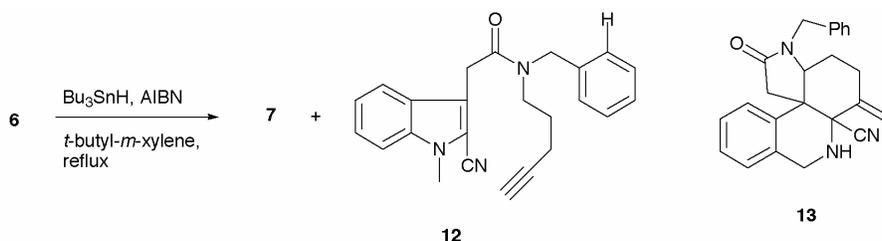
Results and Discussion

The required cyclisation precursor was synthesized following our previous approach from the sulfonamide **8** which utilized the work of Bowman and Fukuyama for the synthesis of the secondary amine.^{4,5} Reaction of **8** with 4-pentynol under Mitsunobu conditions gave the tertiary sulfonamide **9** in 96% yield (Scheme 3). Deprotection of the tertiary sulfonamide **9** using potassium carbonate and thiophenol gave the secondary amine **10** in 75% yield.⁵ Reaction of this with the acid chloride **11** following our previous work on oxindoles,⁶ gave the cyclisation precursor **6** in 86% yield as a 1:1.3 mixture of amide rotamers (Scheme 3).



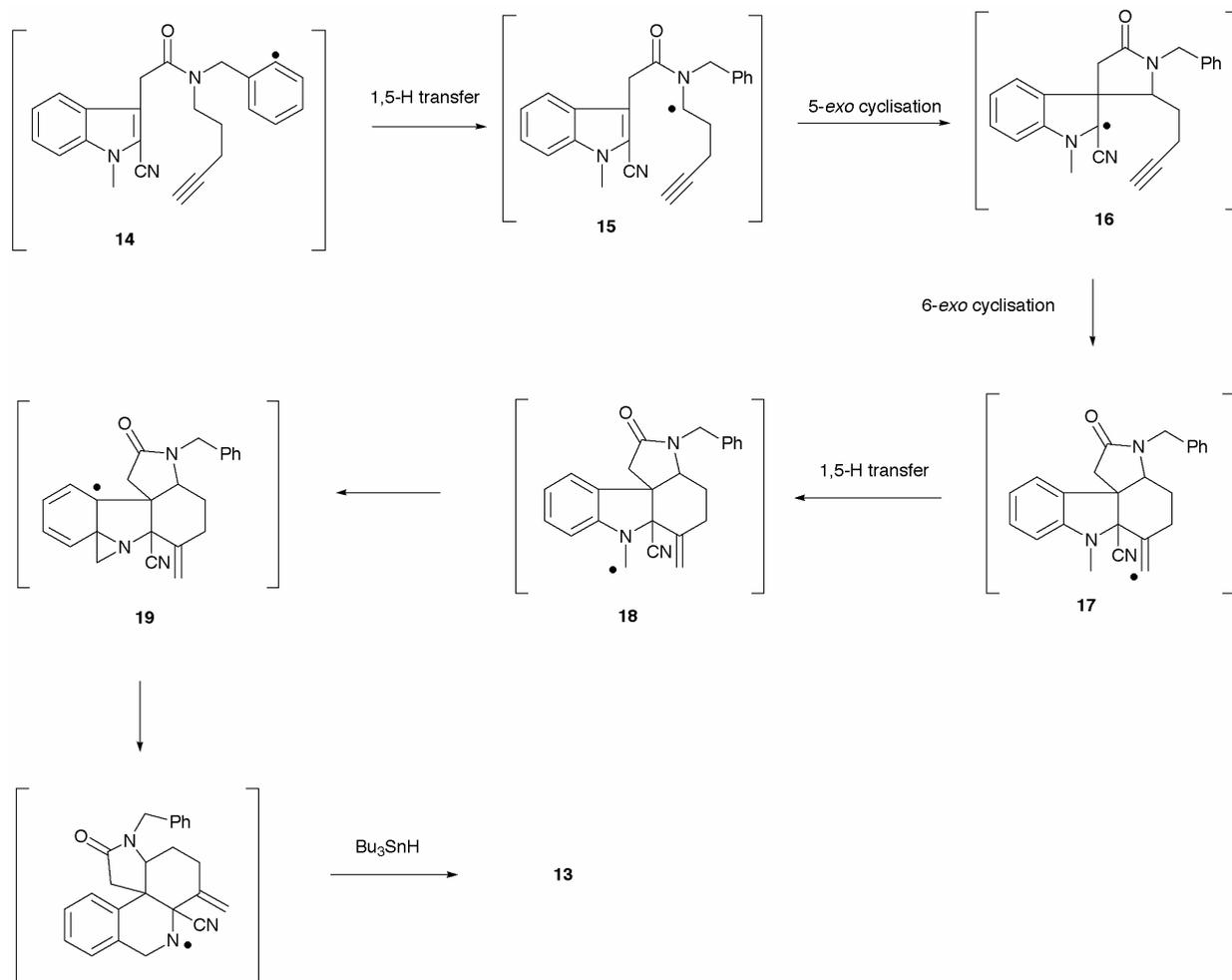
Scheme 3. Reagents and Conditions: (i) PPh_3 , DEAD, THF, $0\text{ }^\circ\text{C}$, 96%; (ii) K_2CO_3 , MeCN, PhSH, 75%; (iii) $i\text{Pr}_2\text{NEt}$, CH_2Cl_2 , $0\text{ }^\circ\text{C}$, 86%.

Following the successful cyclisation of the *N*-pentenyl precursor **4** in our previous example,³ we decided to use the same conditions for cyclisation of the *N*-pentynyl precursor **6**. Treatment of a solution of the tertiary amide **6** in *t*-butyl-*m*-xylene under reflux with syringe pump addition of a solution of tri-*n*-butyltin hydride and AIBN in *t*-butyl-*m*-xylene resulted in the formation of three isolable products. High-resolution mass spectrometry confirmed the same molecular formula for all three compounds, $\text{C}_{24}\text{H}_{23}\text{N}_3\text{O}$. The least polar compound was identified as the reduced product **12** owing to the presence of 9 aromatic protons, the terminal acetylene proton and an equal mixture of amide rotamers in the ^1H NMR spectrum. It was isolated in 45% yield. From the ^{13}C NMR spectrum, the second product isolated in 16% yield clearly possessed an exocyclic double bond (resonance at δ 119.4) along with the distinctive spirocyclic center (δ 53.8), indicating that the precursor **6** had undergone the desired translocation-cyclisation-cyclisation sequence onto the exocyclic triple bond. This along with the other observable data such as two distinct AB quartets in the ^1H NMR clearly indicated that we had indeed synthesized the tetracyclic structure **7**. The relative stereochemistry of this diastereoisomer cannot easily be determined owing to the three contiguous quaternary centers but it appears to be one single diastereoisomer.



Scheme 4

The nature of the third isolable product presented a challenge, as it clearly possessed three AB quartets from the ^1H NMR spectrum. The exocyclic double bond was also present indicating that the final cyclisation step had taken place. From the ^{13}C NMR spectrum there were 5 CH_2 signals excluding the exocyclic methylene group. Eight quaternary carbons were also observed in the ^{13}C NMR spectrum with no evidence for the expected *N*-methyl group in either the ^1H or ^{13}C NMR spectrum. On the basis of the evidence, we have assigned the tetracyclic structure **13** to this compound, which was isolated in 15% yield. The formation of this unexpected product is believed to have occurred by an additional 1,5-hydrogen atom abstraction by the vinylic radical **17** from the neighbouring *N*-methyl group of the indole (Scheme 5). The resultant primary radical **18** then undergoes a neophyl-type rearrangement by addition to the benzene ring to give cyclohexadienyl radical **19**. Ring-opening of **19** to regenerate the aromatic ring gives an aminyl radical which is reduced by tri-*n*-butyltin hydride to give the final compound **13**.



Scheme 5

This unexpected product **13** possesses a novel ring structure which has arisen by a formal ring expansion of an indole to a tetrahydroisoquinoline. The formation of this product is surprising. 1,5-Hydrogen atom abstraction by a vinylic radical is well precedented⁷⁻⁹ as is the neophyl rearrangement involving an aromatic ring with concomitant ring expansion.^{10,11} However, the sequential occurrence of these two reactions as part of a tandem process is unprecedented.

In summary, cyclisation of the *N*-pentynyl precursor **6** results in the formation of the expected cyclised product **7**, carrying suitable functionality for conversion into natural indole alkaloids. In addition, the novel tetracycle **13** has also been isolated. We suggest that this arises through a combination of hydrogen atom abstraction and radical rearrangement.

Experimental Section

General Procedures. ¹H NMR and ¹³C NMR were recorded on a Bruker AM300 spectrometer operating at 300 MHz for proton and 75 MHz for carbon. Infrared spectra were recorded on a Perkin Elmer 1605 FT-IR spectrophotometer using NaCl plates. High resolution mass spectra were carried out at King's College, London University or at Kingston University. Mass spectra carried out at King's College using either a Kratos MS89MS with Kratos DS90 software or a Jeol AX505W with Jeol complement data system. Samples were ionised electronically (EI), with an accelerating voltage of ≈6kV or by low resolution fast atom bombardment (FAB) in a thioglycerol matrix. High resolution fast atom bombardment was carried out at the ULIRS mass spectrometry facility at the School of Pharmacy, University of London. Mass spectra carried out at Kingston University were recorded using a Micromass LCT time of flight mass spectrometer equipped with an ElectroSpray Ionisation (ESI) ion source.

***N*-(2-Bromobenzyl)-2-nitrobenzenesulfonamide (8).** A solution of 2-nitrobenzene sulfonyl chloride (25.00 g, 112.3 mmol) in dichloromethane (100 cm³) was added dropwise to a stirred solution of 2-bromobenzylamine hydrochloride (25.00 g, 112.3 mmol) and triethylamine (50.1 cm³, 36.40 g, 360.0 mmol) in dichloromethane (150 cm³) at 0 °C. The resulting solution was allowed to warm to room temperature and stirred for 16 hours, washed with water (3 x 200 cm³), dried (MgSO₄), filtered and organic solvent removed under reduced pressure. The crude product was purified by recrystallisation (ethyl acetate/ hexane) to give *N*-(2-bromobenzyl)-2-nitrobenzenesulfonamide (**8**) as a white crystalline solid (36.63 g, 89%); m.p. 101-103 °C; *R*_f (3: 2, hexane: ethyl acetate) 0.57; (Found MH⁺, 370.9694/ 372.9696, C₁₃H₁₂BrN₂O₄S requires 370.9701/ 372.9681); *v*_{max} /cm⁻¹ 3347.8 (NH), 1531.1 (Ar-NO₂), 1162.6 (NSO₂Ar); *δ*_H(300 MHz; CDCl₃) 4.34 (2H, d, *J* 6.3, CH₂), 6.04 (1H, t, *J* 6.3, NH), 7.00 (1H, td, *J* 7.8 & 1.6, C-4H), 7.13 (1H, td, *J* 7.8 & 1.6, C-5H), 7.29 (1H, dd, *J* 7.8 & 1.6, C-6H), 7.31 (1H, dd, *J* 7.8 & 1.6, C-3H), 7.51 (1H, td, *J* 7.6 & 1.6, C-5'H), 7.58 (1H, td, *J* 7.6 & 1.6, C-4'H), 7.34 (1H, dd, *J* 7.6 & 1.6, C-6'H), 7.83 (1H, dd, *J* 7.6 & 1.6, C-3'H); *δ*_C(75 MHz; CDCl₃) 48.20 (CH₂), 123.60 (C-2),

125.40 (Ar-C-H), 127.63 (Ar-C-H), 129.80 (Ar-C-H), 130.72 (Ar-C-H), 130.92 (Ar-C-H), 132.80 (Ar-C-H), 132.91 (Ar-C-H), 133.61 (Ar-C-H), 133.86 (quaternary C), 134.93 (quaternary C), 147.48 (C-2').

***N*-(2-Bromobenzyl)-2-nitro-*N*-pent-4-ynylbenzenesulfonamide (9).** Diethyl azodicarboxylate (11.20 cm³, 12.38 g, 71.1 mmol) was added dropwise to a solution of *N*-(2-bromobenzyl)-2-nitrobenzenesulfonamide (**8**) (20.30 g, 54.7 mmol), 4-pentyn-1-ol (6.1 cm³, 5.52 g, 65.6 mmol) and triphenylphosphine (18.64 g, 71.1 mmol) in THF (150 cm³) at 0 °C. The reaction was allowed to warm to room temperature and stirred overnight. Organic solvent was removed under reduced pressure and the residue taken up in diethyl ether (70 cm³). The volume of the solution was reduced and the solution filtered to remove triphenylphosphine oxide. The filtrate was reduced in volume and the yellow oil purified by flash column chromatography (3: 2, hexane: ethyl acetate) to give the title compound (**9**) as a light yellow oil (22.96 g, 96%); R_f (3: 2, hexane: ethyl acetate) 0.55; (Found MH⁺, 437.0156/ 439.0169, C₁₈H₁₈BrN₂O₄S requires 437.0171/ 439.0150); ν_{max}/cm⁻¹ 3300.4 (CCH), 3061.0, 2942.5 (Ar-H), 1544.7 (Ar-NO₂), 1371.4 (NSO₂Ar), 1163.8 (NSO₂Ar); δ_H(300 MHz; CDCl₃) 1.61 (2H, m, NCH₂CH₂), 1.87 (1H, t, *J* 2.6, CCH), 2.04 (2H, td, *J* 7.0 & 2.6, CH₂CH₂CCH), 3.39 (2H, t, *J* 7.6, NCH₂CH₂), 4.66 (2H, s, NCH₂Ar), 7.09 (1H, td, *J* 7.6 & 1.6, C-4H), 7.23 (1H, td, *J* 7.6 & 1.6, C-5H), 7.42 (1H, dd, *J* 7.6 & 1.6, C-6H), 7.47 (1H, dd, *J* 7.6 & 1.6, C-3H), 7.60-7.70 (3H, m, Ar-H), 7.96 (1H, m, Ar-H); δ_C(75 MHz; CDCl₃) 15.73 (CH₂), 26.78 (CH₂), 47.28 (NCH₂CH₂), 51.48 (NCH₂Ar), 69.44 (CCH), 82.69 (CCH), 123.32 (C-2), 124.33 (Ar-C-H), 127.91 (Ar-C-H), 129.47 (Ar-C-H), 129.80 (Ar-C-H), 130.86 (Ar-C-H), 132.04 (Ar-C-H), 132.96 (Ar-C-H), 133.09 (C-1), 133.96 (Ar-C-H), 135.02 (C-1'), 147.88 (C-2').

***N*-(2-Bromobenzyl)pent-4-ynylamine (10).** Thiophenol (5.9 cm³, 6.36 g, 57.8 mmol) was added to a stirred solution of sulfonamide (**9**) (22.95 g, 52.5 mmol) and potassium carbonate (23.58 g, 170.6 mmol) in acetonitrile (150 cm³) at room temperature. The resulting solution was left to stir overnight at room temperature. Organic solvent was removed under reduced pressure and the residue was taken up in diethyl ether (200 cm³). Hydrochloric acid (2.0 M solution) was added until the solution remained acidic and the resulting solution stirred for ten minutes. The organic layer was separated and washed with dilute hydrochloric acid (100 cm³ of a 1.0 M solution). The combined aqueous phases were washed with diethyl ether (200 cm³) and made basic by the addition of solid potassium carbonate. The aqueous solution was extracted with diethyl ether (4 x 150 cm³) and the combined extracts washed with brine (200 cm³), dried (MgSO₄), filtered and evaporated to dryness under reduced pressure to give the title compound (**10**) as a pale yellow oil (9.94 g, 75%); R_f (3: 2, hexane: ethyl acetate) 0.21; (Found MH⁺, 252.0377/ 254.0381, C₁₂H₁₅BrN requires 252.0388/ 254.0367); ν_{max}/cm⁻¹ 3422.5 (NH), 3301.6 (CCH); δ_H(300 MHz; CDCl₃) 1.39 (1H, br s, NH), 1.64 (2H, quin, *J* 7.0, NHCH₂CH₂), 1.86 (1H, t, *J* 2.6, CCH), 2.19 (2H, td, *J* 7.0 & 2.6, CH₂CCH), 2.64 (2H, t, *J* 7.0, NCH₂CH₂), 3.76 (2H, s, NCH₂Ar), 7.01 (1H, td, *J* 7.5 & 1.0, C-4H), 7.17 (1H, td, *J* 7.5 & 1.0, C-5H), 7.29 (1H, dd, *J* 7.5 & 1.0, C-6H), 7.43 (1H, dd, *J* 7.5 & 1.0, C-3H); δ_C(75 MHz; CDCl₃) 16.61 (CH₂), 28.75 (CH₂),

47.92 (NCH₂CH₂), 53.65 (NCH₂Ar), 68.61 (CCH), 84.08 (CCH), 123.94 (C-2), 127.39 (C-5), 128.52 (C-4), 130.19 (C-6), 132.75 (C-3), 139.34 (C-1).

***N*-(2-Bromobenzyl)-2-(2-cyano-1-methyl-1*H*-indol-3-yl)-*N*-pent-4-ynylacetamide (6).** A solution of acid chloride (**11**) (3.25 g, 14.0 mmol) in dichloromethane (50 cm³) was added dropwise *via* cannula to a stirred solution of (2-bromobenzyl)-pent-4-ynylamine (**10**) (4.58 g, 18.15 mmol) and *N,N*-diisopropylethylamine (8.5 cm³, 6.31 g, 48.9 mmol) in dichloromethane (100 cm³) at 0 °C under nitrogen. The resulting mixture was left to stir at 0 °C for one hour, allowed to warm to room temperature and then left to stir overnight. Organic solvent was removed under reduced pressure and the residue taken up in dichloromethane (200 cm³), washed with HCl (200 cm³ of a 0.5 M solution), saturated sodium hydrogen carbonate (200 cm³) and brine (200 cm³). The organic phase was dried (MgSO₄), filtered and solvent removed under reduced pressure to give a light green solid which was purified by flash column chromatography (2: 1, hexane: ethyl acetate) to give the tertiary amide (**6**) as a light yellow solid and as a 1: 1.3 ratio of amide rotamers (5.40 g, 86%); m.p. 119-120 °C; R_f (2: 1, hexane: ethyl acetate) 0.83; (Found M⁺, 447.0956/ 449.0916, C₂₄H₂₂BrN₃O requires 447.0947/ 449.0927); ν_{max}/cm⁻¹ 3303.1 (CCH), 3012.8 (Ar-H), 2217.6 (CN), 1653.9 (CONR₂); δ_H(300 MHz; CDCl₃) 1.96 (2H, quin, *J* 6.8, C-2''H₂ (major + minor)), 2.08 (0.4H, t, *J* 2.4, C-5''H (minor)), 2.17 (0.6H, t, *J* 2.4, C-5''H (major)), 2.34 (1.2H, td, *J* 6.8 & 2.4, C-3''H₂ (major)), 2.40 (0.8H, td, *J* 6.8 & 2.4, C-3''H₂ (minor)), 3.64 (2H, m, C-1''H₂ (major + minor)), 3.83 (1.8H, s, NCH₃ (major)), 3.97 (1.2H, s, NCH₃ (minor)), 4.02 (1.2H, s, CH₂CO (major)), 4.25 (0.8H, s, CH₂CO (minor)), 4.82 (1.2H, s, NCH₂Ar (major)), 4.88 (0.8H, s, NCH₂Ar (minor)), 6.92 (0.4H, m, Ar-H (minor)), 7.04-7.42 (5.6H, m, Ar-H (major + minor)), 7.49 (0.4H, d, *J* 8.0, Ar-H (minor)), 7.70 (0.6H, m, Ar-H (major)), 7.76 (0.6H, d, *J* 8.0, Ar-H (major)), 7.89 (0.4H, d, *J* 8.0, Ar-H (minor)); δ_C(75 MHz; CDCl₃) 15.86 (CH₂), 16.17 (CH₂), 26.33 (CH₂), 27.36 (CH₂), 30.76 (CH₂), 31.09 (CH₂), 31.41 (NCH₃), 31.62 (NCH₃), 46.50 (CH₂), 46.78 (CH₂), 48.65 (CH₂), 52.57 (CH₂), 69.12 (C-4''), 70.00 (C-4''), 82.72 (C-5''), 83.40 (C-5''), 109.82 (C-3), 110.06 (C-7), 110.14 (C-7), 112.93 (CN), 113.32 (CN), 120.09 (quaternary C), 120.69 (quaternary C), 121.08 (Ar-C-H), 121.18 (Ar-C-H), 121.43 (Ar-C-H), 122.60 (quaternary C), 123.50 (quaternary C), 126.07 + 126.22 + 126.77 + 127.66 + 127.33 + 128.85 + 128.99 + 129.21 + 132.75 + 133.08 (Ar-C-H), 135.33 (quaternary C), 136.25 (quaternary C), 137.96 (quaternary C), 138.14 (quaternary C), 169.43 (CO), 169.84 (CO); *m/z* 449.09 (18.8%, M⁺ ⁸¹Br), 447.10 (20.6, M⁺ ⁷⁹Br), 368.17 (62.9), 183.09 (59.2), 170.99 (91.8), 170.10 (66.6), 169.09 (100.0), 168.08 (43.3), 91.06 (49.9), 90.05 (56.0).

Radical cyclisation of *N*-(2-bromobenzyl)-2-(2-cyano-1-methyl-1*H*-indol-3-yl)-*N*-pent-4-ynylacetamide (6). A solution of tri-*n*-butyltin hydride (0.75 cm³, 0.81 g, 2.78 mmol) and azo-bis-isobutyronitrile (AIBN) (0.048 g, 2.78 mmol) in *t*-butyl-*m*-xylene (30 cm³) were added dropwise *via* syringe pump (6.37 cm³/hour) to a solution of the amide (**6**) (1.039 g, 2.32 mmol) in *t*-butyl-*m*-xylene (90 cm³) at reflux. Once addition was complete, heating was continued for 2 hours. The reaction was allowed to cool and organic solvent removed under reduced pressure and the residue taken up in acetonitrile (50 cm³) and extracted with hexane (4 x 50 cm³). The

acetonitrile was removed under reduced pressure and the residue purified by multiple flash column chromatography (3: 1, hexane: ethyl acetate) to give a mixture of three products:

***N*-benzyl-2-(2-cyano-1-methyl-1H-indol-3-yl)-*N*-(pent-4-ynyl)acetamide (12).** White solid as a 1: 1 mix of amide rotamers (0.38 g, 45%); m.p. 82-84 °C; (Found M^+ , 369.18510, $C_{24}H_{23}N_3O$ requires 369.18411); ν_{\max} / cm^{-1} 3296.7 (CCH), 3059.2, 3030.5, 2938.7 (Ar-H), 2217.5 (CN), 1648.6 (CONR₂); δ_H (300 MHz; $CDCl_3$) 1.81 (2H, quin, J 7.0, C-2''H₂), 1.94 (0.5H, t, J 2.5, CCH), 2.05 (0.5H, t, J 2.5, CCH), 2.19 (1H, td, J 7.0 & 2.5, C-3''H₂), 2.26 (1H, td, J 7.0 & 2.5, C-3''H₂), 3.51 (2H, m, C-1''H₂), 3.72 (1.5H, s, NCH₃), 3.85 (1.5H, s, NCH₃), 3.96 (1H, s, CH₂CO), 4.09 (1H, s, CH₂CO), 4.65 (1H, s, CONCH₂Ar), 4.72 (1H, s, CONCH₂Ar), 7.09-7.44 (8H, m, Ar-H), 7.69 (0.5H, d, J 8.1, Ar-H), 7.77 (0.5H, d, J 8.1, Ar-H); δ_C (75 MHz; $CDCl_3$) 15.80 (CH₂), 16.14 (CH₂), 26.28 (CH₂), 27.15 (CH₂), 30.77 (CH₂), 31.27 (CH₂), 31.44 (NCH₃), 31.62 (NCH₃), 46.15 (CH₂), 46.37 (CH₂), 48.72 (CH₂), 51.91 (CH₂), 69.12 (CCH), 69.94 (CCH), 82.84 (CCH), 83.54 (CCH), 109.76 (C-3), 110.05 (C-7), 110.15 (C-7), 113.21 (CN), 113.38 (CN), 120.48 (quaternary C), 120.91 (quaternary C), 121.20 (Ar-C-H), 121.29 (Ar-C-H), 121.43 (Ar-C-H), 125.93 (Ar-C-H), 126.05 (Ar-C-H), 126.14 (Ar-C-H), 126.20 (Ar-C-H), 127.43 (Ar-C-H), 127.48 (Ar-C-H), 128.18 (Ar-C-H), 128.35 (quaternary C), 128.60 (Ar-C-H), 128.82 (Ar-C-H), 136.53 (quaternary C), 137.39 (quaternary C), 138.02 (quaternary C), 138.15 (quaternary C), 169.27 (CO), 169.71 (CO); m/z 369.19 (43.6%, M^+), 321.23 (11.4), 273.13 (77.2), 169.08 (90.9), 168.08 (56.6), 121.06 (79.9), 91.04 (81.4), 77.04 (37.6).

1-Benzyl-8-methyl-9-methylene-2-oxo-2,3,8,8a,9,10,11,11a-octahydro-1H-pyrrolo[2,3-d]carbazole-8a-carbonitrile (7). Colourless oil (0.14 g, 16%); (Found M^+ , 369.18666, $C_{24}H_{23}N_3O$ requires 369.18411); ν_{\max} / cm^{-1} 2924.4, 2854.8 (Ar-H), 2218.2 (CN), 1694.1 (CONR₂); δ_H (300 MHz; CD_3OD) 1.32 (1H, m, NCHCH₂), 2.16-2.28 (2H, m, NCHCH₂ & NCHCH₂CH₂), 2.39 (1H, m, NCHCH₂CH₂), 2.63 (3H, s, NCH₃), 2.69 & 2.93 (2H, ABq, CH₂CO), 3.13 (1H, dd, J 5.4, NCH), 4.11 & 4.76 (2H, ABq, J 14.7, CONCH₂Ar), 5.49 (1H, d, J 1.3, CCH₂), 5.63 (1H, s, CCH₂), 6.67 (1H, d, J 7.5, C-7H), 6.76 (1H, td, J 7.5 & 1.0, C-6H), 6.94 (1H, d, J 7.4, C-4H), 7.16 (1H, td, J 7.5 & 1.0, C-5H), 7.20 (5H, m, Ar-H); δ_C (75 MHz; CD_3OD) 25.53 (CH₂), 29.38 (CH₂), 30.69 (NCH₃), 38.38 (CH₂), 45.77 (CH₂), 53.84 (quaternary C), 65.02 (NCH), 78.91 (quaternary C), 110.57 (C-7), 116.90 (CN), 119.43 (CCH₂), 121.58 (Ar-C-H), 122.59 (Ar-C-H), 128.87 (Ar-C-H), 129.62 (2 x Ar-C-H), 129.69 (2 x Ar-C-H), 130.55 (Ar-C-H), 134.66 (quaternary C), 137.19 (quaternary C), 140.86 (quaternary C), 149.83 (quaternary C), 173.36 (CO); m/z 369.19 (100.0%, M^+), 360.95 (16.4), 266.99 (24.4), 169.08 (35.8), 149.02 (32.9), 91.06 (86.6), 83.09 (35.2).

12-Benzyl-3-methylene-11-oxo-1,2,3,3a,4,5,10,11,12,12a-decahydropyrrolo[2,3-n]phenanthridine-3a-carbonitrile (13). White solid (0.13 g, 15%); m.p. 195-197 °C; (Found M^+ , 369.18407, $C_{24}H_{23}N_3O$ requires 369.18411); δ_H (300 MHz; $CDCl_3$) 1.71-1.62 (1H, m, NCHCH₂), 1.97-1.85 (1H, m, NCHCH₂), 2.35 (2H, m, NCHCH₂CH₂), 2.84 & 2.98 (2H, ABq, J 17.5, CH₂CO), 3.37 (1H, dd, J 12.6 & 3.3, NCH₂), 3.52 (1H, d, J 12.6, NCH₂), 3.54 (1H, t, J 5.3, NCH), 4.04 (1H, d, J 14.9, CONCH₂Ar), 4.19 (1H, br s, NH), 4.96 (1H, d, J 14.9, CONCH₂Ar), 5.31 (1H, s, CCH₂), 5.62 (1H, s, CCH₂), 6.54 (1H, d, J 7.5, C-7H), 6.69 (1H, td, J 7.5 & 1.0, C-

5H), 7.01-7.07 (2H, m, Ar-H), 7.13-7.24 (5H, m, Ar-H); δ_{C} (75 MHz; CDCl₃) 24.57 (CH₂), 25.38 (CH₂), 42.91 (CH₂), 43.01 (quaternary C), 44.70 (CH₂), 45.65 (quaternary C), 48.91 (CH₂), 62.13 (NCH), 115.54 (C-7), 116.99 (CCH₂), 119.20 (Ar-C-H), 120.12 (quaternary C), 125.53 (quaternary C), 126.58 (Ar-C-H), 127.75 (Ar-C-H), 128.35 (2 x Ar-C-H), 128.55 (Ar-C-H), 128.62 (2 x Ar-C-H), 135.67 (quaternary C), 140.27 (quaternary C), 140.87 (quaternary C), 172.60 (CO); m/z 369.18 (48.0%, M⁺), 303.15 (21.7), 266.99 (27.8), 245.11 (29.2), 169.08 (53.2), 91.06 (28.8).

Acknowledgements

We wish to acknowledge Kingston University for the financial support to carry out this research.

References and Footnotes

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