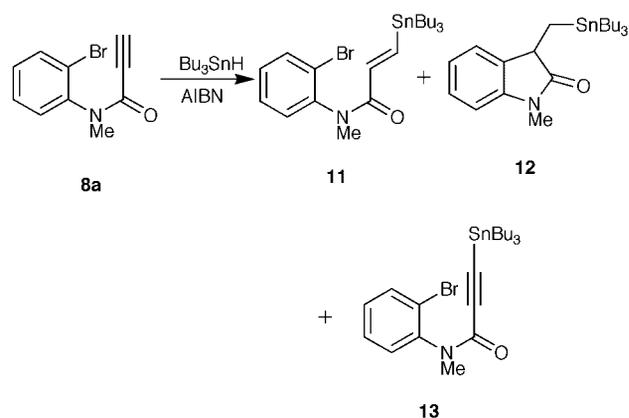


Scheme 4



Scheme 5

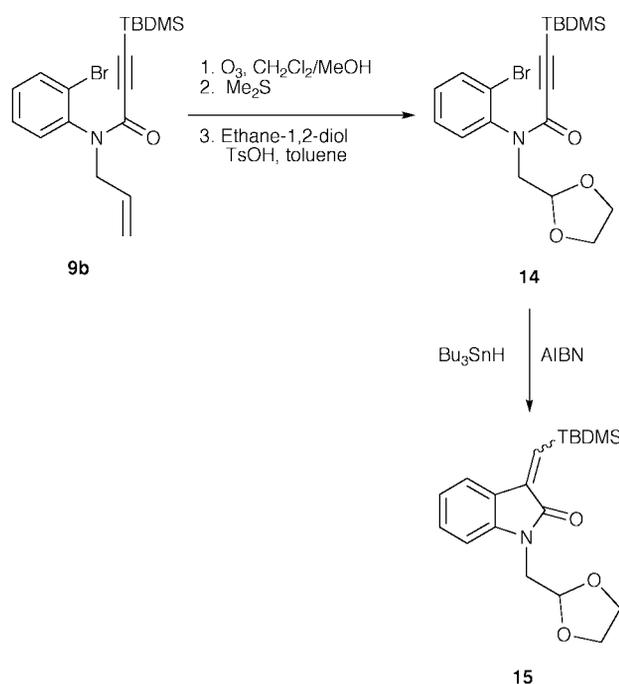
Reaction of the alkyne with TBTH was clearly a major problem. In order to explore this reaction further, a range of amides **8** and **9** were synthesised. The obvious way to slow down this unwanted reaction was to introduce a substituent onto the terminus of the alkyne. The simplest substituent to introduce was a methyl group although this would not be suitable for the formation of the C-9 carbamate of the mitomycins. 2-Bromoaniline was reacted with but-2-ynoic acid using DCC to give butynamide **7b** in 21% yield. *N*-Methylation under the usual conditions gave **8b** in 72% yield. To fulfill the long-term aim of the project, a removable group was required on the terminus of the alkyne and a silyl group was chosen.¹⁰ Initial studies using the trimethylsilyl group proved unsuccessful at the radical cyclisation stage and so attention was turned to the bulkier *tert*-butyldimethylsilyl (TBDMS) group. In addition, we introduced an *N*-allyl group into the cyclisation precursors to provide a basis for the synthesis of the third ring of the mitomycins. Reaction of **7a** with allyl bromide using sodium hydride as base gave the desired *N*-allyl amide **8c** in a poor 18% yield. This was improved to 68% by using allyl triflate in place of the bromide. Silylation of **8a** and **8c** was achieved in 98% and 99% yields respectively using lithium hexamethyldisilazide at $-78\text{ }^{\circ}\text{C}$ with addition of *tert*-butyldimethylsilyl chloride and warming to room temperature. With reliable syn-

Table 1 Ratio of 3-methyleneindol-2(3*H*)-one isomers produced in the radical cyclisation in Scheme 7

R ¹	R ²	Ratio <i>E</i> : <i>Z</i>	Combined yield (%)
Me	TBDMS	1:3	62
Allyl	TBDMS	1:4.7	59
CH ₂ -Dioxolane	TBDMS	1:3.5	67

theses of **8b**, **9a** and **9b** completed, the radical cyclisation was studied.

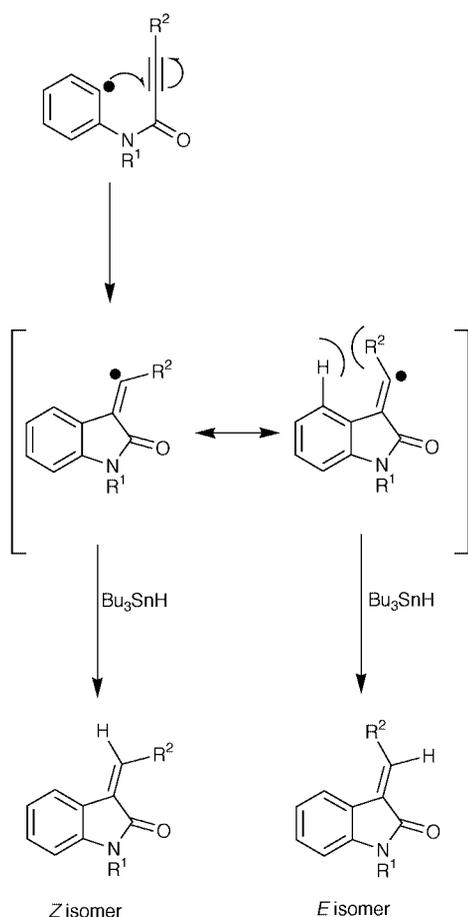
Radical cyclisation of **8b** under the normal radical conditions gave an inseparable mixture of three products which were tentatively assigned as the *Z*- and *E*-isomers of **10a** along with starting material in combined 40% yield. Evidence for the cyclised products was obtained from the mass spectrum which showed M^+ , 173. The presence of unreacted starting material is indicative of a poor radical chain presumably owing to the relatively slow addition of the nucleophilic aryl radical to the carbon-carbon triple bond. Consequently, in the reactions of **9a** and **9b**, 10 mol% of AIBN was added every hour for 3 hours to overcome this problem. In this way reasonable yields of cyclised products were obtained which consisted of separable mixtures of *E*- and *Z*-isomers of the desired methylene oxindoles **10**. The results are summarised in Table 1. The isomers were assigned on the basis of NOE experiments which showed an enhancement between the olefinic proton and an aromatic proton in the *Z*-isomers. Simultaneously a cyclisation substrate was prepared which we envisaged would lead to the synthesis of the pyrroloindole skeleton of mitomycin. This involved aryl radical cyclisation of an anilide carrying a protected acetaldehyde unit on the nitrogen (Scheme 6). The cyclisation precursor **14** was prepared by ozonolysis of **9b** followed by protection of the aldehyde using ethane-1,2-diol. Radical cyclisation then afforded the *E*- and *Z*-isomers of oxindole **15** in a combined 67% yield (see Table 1).



Scheme 6

In all the cyclisations studied, the *Z*-isomer of the 3-methylene oxindole was the major product. The intermediate vinyl radical is not configurationally stable,¹¹ therefore a mixture of *E*- and *Z*-isomers around the double bond was

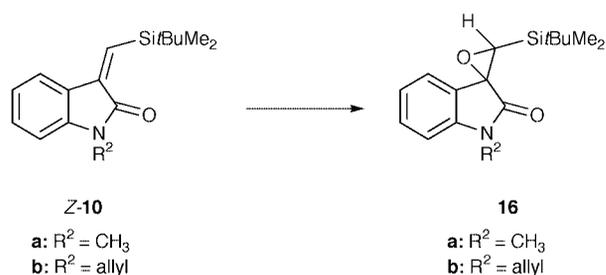
expected. It seems likely that an unfavourable steric interaction between R^2 and the C-4 hydrogen leads to preferential formation of the less hindered *Z*-isomer (Scheme 7). The



Scheme 7

bulky TBDMS group would be expected to be particularly discriminating in this respect.

In order to introduce the C-9 carbamate group found in the mitomycins, oxygenation of the exocyclic double bond of the 3-methylene oxindoles is required. The reactivity of this alkene is not clear as it is conjugated to the carbonyl group but carries an electron-donating silyl group. Initial attempts to epoxidise the *Z*-isomer of **10b** using base-catalysis and either hydrogen peroxide or *tert*-butyl hydroperoxide failed. However reaction with excess *m*-chloroperoxybenzoic acid (MCPBA) gave the epoxide **16a** in 43% yield along with recovered starting material (Scheme 8). A clear illustration of the reactivity of this alkene



Scheme 8

was obtained when the *Z*-isomer of **10c** carrying an *N*-allyl group was epoxidised in the same manner to give epoxide **16b** in 51% yield with 40% recovered starting material.

In conclusion we have shown that the facile 5-*exo-dig* aryl radical cyclisation provides a concise route to novel

silyl-substituted methylene indol-2-ones. The epoxidation of these systems can be achieved using MCPBA.

Experimental

General conditions

^1H and ^{13}C NMR spectra were recorded on a Bruker AM360 spectrometer at 360 and 90 MHz respectively or on a Bruker AM400 spectrometer at 400 and 100 MHz respectively using CDCl_3 as solvent with SiMe_4 as an internal standard, unless otherwise stated. *J*-Values are given in Hz. IR spectra were recorded on a Perkin-Elmer Paragon 1000 Infrared spectrometer, using Nujol mulls or dichloromethane solutions unless otherwise stated. All values in cm^{-1} . Data are presented where w, m, s, represent weak, medium and strong absorptions respectively. Mass spectral data was recorded on a JEOL AX505W with complement data system. Samples were ionised electronically at 70 eV with typical accelerating voltage of 6 kV. Melting points were determined using a Kofler hot plate apparatus and are uncorrected. All column chromatography was carried out using the flash chromatography technique of Still, using Merck 60 (230–400 mesh) silica gel. Analytical TLC was carried out on Merck plastic backed TLC plates, coated with silica gel 60 F-254. Plates were visualised using ultraviolet light, unless otherwise stated. Eluting solvent systems are stated where appropriate. All dry reactions were performed in an inert argon atmosphere using a vacuum–argon manifold for the exclusion of water. Stirring was by internal magnetic bead. All syringes, needles and glassware were pre-dried at 110°C and cooled in an anhydrous atmosphere before use. Diethyl ether, THF, and toluene were pre-dried over Na wire and refluxed over Na under Ar with benzophenone as an indicator in the reaction vessel. Dichloromethane was refluxed under Ar, over CaH_2 and distilled directly into the reaction vessel.

Tri-*n*-butylstannane. This was prepared by the method of Szammer and Otvos.¹² Bis(tri-*n*-butyltin)oxide (50 g, 0.084 mol) was dissolved in absolute ethanol (250 ml) at 0°C under argon. Sodium borohydride (2.22 g, 0.059 mol) was added and the reaction allowed to warm to room temperature then stirred for one hour. The ethanol was removed *in vacuo* and the resultant white slurry was dissolved in hexane, washed with water (3×50 ml), dried (MgSO_4) and evaporated under reduced pressure. The resultant liquid was rapidly distilled under reduced pressure. Yield: 90%. R_f (hexane) 0.83; δ_{H} (360 MHz; CDCl_3) 0.92 (9H, t, *J* 7.3, $3 \times \text{CH}_3$), 1.27–1.41 (12H, m, $3 \times \text{H}-1 + 3 \times \text{H}-3$), 1.60–1.69 (6H, m, $3 \times \text{H}-2$), 5.29 (1H, t, *J* 1.0, Sn-H).

Preparation of amides: general procedure

2-Bromoaniline was added to a solution of the acid in dichloromethane. A solution of DCC in dichloromethane was then added dropwise at 0°C . The resulting solution was stirred for 30 minutes after which time a white precipitate formed. The reaction mixture was stirred for a further 3 hours at room temperature, then cooled in ice and filtered, the residue was washed with dichloromethane. The filtrate was washed with 2 M HCl (3×200 ml), then with sodium hydrogen carbonate solution (3×200 ml) and water (3×200 ml). The organic layer was dried (MgSO_4) and evaporated under reduced pressure.

***N*-(2'-Bromophenyl)propionamide, 7a.** 2-Bromoaniline (40.5 g, 0.235 mol) and propionic acid (15 g, 0.214 mol) gave the amide **7a** as a white solid (36 g, 75%) after chromatography (SiO_2 , 7% EtOAc–hexane); mp $96\text{--}98^\circ\text{C}$ (Found: C, 47.89; H, 2.59; N, 6.09%. $\text{C}_9\text{H}_6\text{BrNO}$ requires C, 48.25; H, 2.70; N, 6.25%); R_f (30% EtOAc–hexane) 0.33; $\nu_{\text{max}}/\text{cm}^{-1}$ 3288 (m, acetylenic C–H), 3199 (m, secondary amide N–H), 2110 (s, acetylenic C=C), 1633 (s, amide C=O); δ_{H} (360 MHz; CDCl_3) 8.29 (1H, d,

J 8.0, H-6'), 7.96 (1H, br s, N-H), 7.56 (1H, d, J 8.0, H-3'), 7.33 (1H, t, J 8.0, H-5'), 7.02 (1H, t, J 8.0, H-4'), 3.01 (1H, s, H-3); $\delta_{\text{C}}(\text{CDCl}_3)$ 149.5 (C=O), 134.9 (C-1'), 132.4 (C-6'), 128.6 (C-3'), 126.1 (C-5'), 122.3 (C-4'), 113.2 (C-2'), 81.5 (HC≡C), 74.8 (HC≡C); m/z 225 (63.3%, ^{81}Br , M^+), 223 (63.3%, ^{79}Br , M^+) 173 (62.4, $\text{M}^+ - \text{C}_3\text{O}$, ^{81}Br), 171 (65.2, $\text{M}^+ - \text{C}_3\text{O}$, ^{79}Br), 144 (94.8, $\text{M}^+ - \text{Br}$), 64 (100) (Found: M^+ (^{79}Br) 222.9632. $\text{C}_9\text{H}_6^{79}\text{BrNO}$ requires M 222.9633).

***N*-(2'-Bromophenyl)but-2-ynamide, 7b.** 2-Bromoaniline (4.5 g, 26 mmol) and butynoic acid (2 g, 23 mmol) gave a white solid which was recrystallised from EtOAc and hexane to give **7b** (1.2 g, 21%), mp 78–79 °C (Found: C, 50.29; H, 3.22; N, 5.72%. $\text{C}_{10}\text{H}_8\text{BrNO}$ requires C, 50.45; H, 3.39; N, 5.88%); R_{f} (30% EtOAc–hexane) 0.26; $\nu_{\text{max}}/\text{cm}^{-1}$ 2235 (C≡C) 1741 (secondary amide C=O); δ_{H} (360 MHz; CDCl_3) 8.31 (1H, d, J 8.5, H-6'), 7.85 (1H, br s, NH), 7.53 (1H, dd, J 8.5, 1.3, H-3'), 7.31 (1H, td, J 8.5, 1.3, H-5'), 6.99 (1H, t, J 8.5, H-4'), 2.03 (3H, s, Me); $\delta_{\text{C}}(\text{CDCl}_3)$ 150.9 (C=O), 135.3 (C-1'), 132.3 (C-6'), 128.4 (C-3'), 125.6 (C-5'), 122.1 (C-4'), 112.9 (C-2'), 85.3 (CH₃), 81.5 (C≡C-CH₃), 75.2 (C≡C-CH₃); m/z 237 (8.3%, M^+ , ^{79}Br), 239 (6.6, M^+ , ^{81}Br), 158 (60.4, $\text{M}^+ - \text{Br}$), 144 (41.7, $\text{M}^+ - \text{BrN}$), 131 (97, $\text{M}^+ - \text{CHBrN}$), 119 (100, $\text{M}^+ - \text{C}_2\text{HBrN}$) (Found M^+ (^{79}Br) 236.9793. $\text{C}_{10}\text{H}_8^{79}\text{BrNO}$ requires M 236.9789).

Preparation of *N*-alkyl amides: general procedure

The amide in THF was added to a stirred suspension of sodium hydride (1.1 equivalents) in THF at 0 °C under argon. The reaction was allowed to stir for 1 hour after which time hydrogen evolution had ceased. The alkyl halide was then added and the reaction allowed to stir at room temperature overnight. The THF was removed *in vacuo* and the resultant solid dissolved in ether (200 ml), then washed with water (3 × 200 ml). The ethereal layer was dried (MgSO_4) and evaporated under reduced pressure.

***N*-(2'-Bromophenyl)-*N*-methylpropynamide, 8a.** Amide **7a** (9 g, 40 mmol) and methyl iodide (5.7 g, 40 mmol) gave a white solid **8a** (6.7 g, 70%) after chromatography (SiO_2 , 15% EtOAc–hexane), mp 88–89 °C (Found: C, 50.33; H, 3.08; N, 5.74%. $\text{C}_{10}\text{H}_8\text{BrNO}$ requires C, 50.45; H, 3.39; N, 5.88%); R_{f} (30% EtOAc–hexane) 0.22; $\nu_{\text{max}}/\text{cm}^{-1}$ 3216 (s, acetylenic C–H), 2103 (s, acetylenic C≡C) 1639 (s, C=O); δ_{H} (360 MHz; CDCl_3) 7.68 (1H, dd, J 7.9, 1.4, H-3'), 7.21–7.43 (3H, m, H-4', H-5', H-6'), 3.26 (3H, s, NMe), 2.75 (1H, s, H-3); $\delta_{\text{C}}(\text{CDCl}_3)$ 153.2 (C=O), 141.4 (C-1'), 133.6 (C-3'), 130.3 (C-5', C-6'), 128.6 (C-4'), 123.6 (C-2'), 79.9 (HC≡C), 75.9 (HC≡C), 35.2 (N-Me); m/z 239, (0.6%, ^{81}Br , M^+), 237 (2.3, ^{79}Br , M^+), 186 (53.6%, $\text{M}^+ - \text{C}_3\text{HO}$, ^{81}Br), 184 (30.1, $\text{M}^+ - \text{C}_3\text{HO}$, ^{81}Br), 157 (17.6, $\text{M}^+ - \text{C}_4\text{H}_4\text{NO}$, ^{81}Br) 155 (22.7, $\text{M}^+ - \text{C}_4\text{H}_4\text{NO}$, ^{79}Br) (Found: M^+ (^{79}Br) 236.9878. $\text{C}_{10}\text{H}_8^{79}\text{BrNO}$ requires M 236.9789).

***N*-(2'-Bromophenyl)-*N*-methylbutynamide, 8b.** Amide **7b** (1.2 g, 5.1 mmol) and methyl iodide (0.78 g, 5.5 mmol) gave **8b** as a white solid, (0.92 g, 72%), mp 61–63 °C (Found: C, 52.36; H, 3.77; N, 5.46%. $\text{C}_{11}\text{H}_{10}\text{BrNO}$ requires C, 52.41; H, 3.96; N, 5.56%); R_{f} (30% EtOAc–hexane) 0.31; $\nu_{\text{max}}/\text{cm}^{-1}$ 2233 (C≡C), 1642 (tertiary amide C=O); δ_{H} (360 MHz; CDCl_3) 7.67 (1H, dd, J 8.0, 1.5, H-3'), 7.39 (1H, td, J 7.8, 1.4, H-5'), 7.26 (2H, m, H-4' + H-6'), 3.48 (s, NMe minor rotamer), 3.23 (3H, s, NMe), 2.09 (s, CH₃, minor rotamer), 1.70 (3H, s, CH₃); $\delta_{\text{C}}(\text{CDCl}_3)$ 154.4 (C=O), 142.0 (C-1'), 133.7 (C-3' minor rotamer), 133.5 (C-3'), 130.4 (C-5'), 129.9 (C-6'), 129.5 (minor rotamer), 129.3 (minor rotamer) 128.7 (minor rotamer), 128.5 (C-4'), 123.6 (C-2'), 89.4 (C≡C-CH₃), 73.7 (C≡C-CH₃) 38.9 (NCH₃ minor rotamer), 35.1 (NCH₃), 4.2 (C≡CCH₃ minor rotamer), 3.8 (C≡CCH₃); m/z 253 (3.2%, M^+ , ^{81}Br), 251 (1.0, M^+ , ^{79}Br), 172 (35.6, $\text{M}^+ - \text{Br}$), 83.8 (100, $\text{M}^+ - \text{C}_6\text{H}_4\text{BrN}$) (Found: M^+ (^{79}Br) 250.9951. $\text{C}_{11}\text{H}_{10}^{79}\text{BrNO}$ requires M 250.9945).

***N*-(2'-Bromophenyl)-*N*-prop-2-enylpropynamide, 8c.** Amide **7a** (0.95 g, 4.3 mmol) and allyl triflate (2 g, 10.5 mmol) gave **8c** as a brown oil (0.77 g, 68%); R_{f} (30% EtOAc–hexane) 0.33; $\nu_{\text{max}}/\text{cm}^{-1}$ 3289 (acetylenic C–H) 2107 (C≡C), 1650 (tertiary amide C=O); δ_{H} (360 MHz; CDCl_3) 7.68 (1H, dd, J 7.3, 0.9, H-6'), 7.36 (1H, dd, J 7.5, 1.3, H-3'), 7.28 (2H, m, H-4', H-5'), 5.86 (1H, m, H-2''), 5.16, (1H, dd, J 10.0, 1.0, H-3''), 5.09 (1H, dd, J 16.9, 1.0, H-3''), 4.77 (1H, dd, J 14.7, 5.7, H-1''), 3.83 (1H, dd, J 14.7, 7.6, H-1''), 2.74 (1H, s, H-3); m/z 265 (2.2%, M^+ , ^{81}Br), 263 (1.8, M^+ , ^{79}Br), 184 (58.6, $\text{M}^+ - \text{Br}$), 84 (100) (Found: M^+ (^{79}Br) 262.9946. $\text{C}_{12}\text{H}_{10}^{79}\text{BrNO}$ requires M 262.9946).

Silylation of alkynes: general procedure

To a stirred solution of the *N*-alkylated amide in THF at –78 °C under argon was added lithium bis(trimethylsilyl)amide (1.2 equivalents). After 30 minutes *tert*-butyldimethylsilyl chloride was added. The reaction was stirred for 30 minutes then slowly warmed to room temperature over 60 minutes. The reaction mixture was quenched with ammonium chloride and THF was evaporated under reduced pressure. The residue was diluted with ether (100 ml) and washed with water (3 × 100 ml), dried (MgSO_4) and evaporated under reduced pressure.

***N*-(2'-Bromophenyl)-*N*-methyl-3-*tert*-butyldimethylsilylpropynamide, 9a.** Amide **8a** (6 g, 25.2 mmol) and *tert*-butyldimethylsilyl chloride (4.6 g, 30.3 mmol) gave **9a** (8.7 g, 98%) as a white solid, mp 49–51 °C (Found: C, 54.49; H, 6.20; N, 3.92%. $\text{C}_{16}\text{H}_{22}\text{BrNOSi}$ requires C, 54.54; H, 6.29; N, 3.98%); R_{f} (30% EtOAc–hexane) 0.41; $\nu_{\text{max}}/\text{cm}^{-1}$ 2196 (C≡C) 1650 (C=O) 1250 (Si–Me₂); δ_{H} (360 MHz; CDCl_3) 7.53 (1H, dd, J 8.0, 1.4, H-3'), 7.29 (2H, m, H-5', H-6'), 7.24 (1H, m, H-4'), 3.25 (3H, s, NMe), 0.67 (9H, s, Si–^{*t*}Bu), –0.054 (3H, s, SiMe), –0.085 (3H, s, SiMe); $\delta_{\text{C}}(\text{CDCl}_3)$ 153.8 (C=O), 142.0 (C-1'), 133.6 (C-3'), 130.5 (C-5'), 130.1 (C-6'), 128.6 (C-4'), 123.9 (C-2'), 96.9 (HC≡C), 96.4 (HC≡C), 35.2 (Si–^{*t*}Bu), 26.8 (N-Me), 16.2 (C-Me₃), –5.4 (Si-Me₂); m/z 353 (0.5%, ^{81}Br , M^+), 351 (0.1, ^{79}Br , M^+), 272 (100, $\text{M}^+ - \text{Br}$) (Found: M^+ (^{79}Br) 351.0677. $\text{C}_{16}\text{H}_{22}^{79}\text{BrNOSi}$ requires M 351.0654).

***N*-(2'-Bromophenyl)-*N*-prop-2-enyl-3-*tert*-butyldimethylsilylpropynamide, 9b.** Amide **8c** (0.73 g, 2.65 mmol) and *tert*-butyldimethylsilyl chloride (0.5 g, 3.18 mmol) gave **9b** (1.0 g, 99%) as a brown oil; R_{f} (30% EtOAc–hexane) 0.59; $\nu_{\text{max}}/\text{cm}^{-1}$ 1655 (s, tertiary amide C=O), 1252 (s, Si–C); δ_{H} (360 MHz; CDCl_3) 7.65 (1H, dd, J 7.9, 1.3, H-3'), 7.34 (1H, td, J 7.2, 1.4, H-5'), 7.24 (2H, m, H-4' + H-6'), 5.85 (1H, m, H-2''), 5.11 (1H, dd, J 6.9, 1.0, *trans* H-3'') 5.09 (1H, dd, J 14.5, 1.3, *cis* H-3''), 4.75 (1H, ddt, J 14.5, 5.7, 1.5, H-1''), 3.82 (1H, ddt, J 14.5, 7.5, 1.0, H-1''), 0.67 (9H, s, Si(C(CH₃)₃), –0.05 (3H, s, SiCH₃), –0.09 (3H, s, SiCH₃); $\delta_{\text{C}}(\text{CDCl}_3)$ 153.4 (C=O), 140.3 (C-1'), 133.6 (C-3'), 131.8 (C-5' + C-2''), 130.0 (C-6'), 129.7 (C-4'), 124.5 (C-2'), 119.3 (C-3''), 97.1 (C-3), 96.4 (C-2), 50.4 (C-1''), 25.8 (C(CH₃)₃), 16.2 (C(CH₃)₃), –5.38 (2 × CH₃); m/z 379 (0.2%, M^+ , ^{81}Br), 377 (0.2, M^+ , ^{79}Br), 298 (10.1, $\text{M}^+ - \text{Br}$), 84 (100) (Found: M^+ (^{79}Br) 377.0825. $\text{C}_{18}\text{H}_{24}^{79}\text{BrNOSi}$ requires M 377.0811).

***N*-(2'-Bromophenyl)-*N*-(1,3-dioxolan-2-ylmethyl)-3-*tert*-butyldimethylsilylpropynamide, 14.** Amide **9b** (3.5 g, 9 mmol) was dissolved in a mixture of dichloromethane and methanol (5:1, 200 ml) and cooled to –78 °C. A steady stream of ozone was passed through the solution until a blue colour persisted and then for a further 60 minutes. Dimethyl sulfide (1.35 ml, 18 mmol) was added and the solution stirred at room temperature for 16 hours. The solvents were evaporated *in vacuo* and then rapidly chromatographed on silica gel (1:3 ethyl acetate–hexane) to give the aldehyde (2.1 g, 62%) as an un-

stable oil which was immediately reacted with ethane-1,2-diol (0.36 ml, 6.5 mmol), toluene-*p*-sulfonic acid (1 crystal) and toluene (50 ml) in a Dean–Stark apparatus until no more water was collected. The toluene was removed *in vacuo* and the residue chromatographed on silica gel (1:5 ethyl acetate–hexane) to give the *title compound*, **14** as a colourless oil (1.7 g, 85%); R_f (30% EtOAc–hexane) 0.4; $\nu_{\max}/\text{cm}^{-1}$ 2927 (m, C–H), 1652 (s, C=O); δ_{H} (360 MHz; CDCl_3) 7.64 (1H, dd, J 8, 1.5, H-3), 7.48 (1H, dd, J 8, 1.5, H-6), 7.35 (1H, td, J 8, 1.5, H-4), 7.21 (1H, td, J 8, 1.5, H-5), 5.18 (1H, dd, J 5.3, 4.4, H-2''), 4.38 (1H, dd, J 14.2, 4.4, H-1''), 3.90 (4H, m, $\text{OCH}_2\text{CH}_2\text{O}$), 3.25 (1H, dd, J 14.2, 5.3, H-1''), 0.67 (9H, s, $\text{C}(\text{CH}_3)_3$), -0.07 (3H, s, Si– CH_3), -0.09 (3H, s, Si– CH_3); δ_{C} (CDCl_3) 154.0 (C=O), 141.0 (C-1), 133.3 (C-3), 132.2 (C-6), 130.0 (C-5), 128.1 (C-4), 124.1 (C-2), 101.0 (C-2''), 97.0 (C-2'), 96.8 (C-3'), 64.9, 64.8 ($\text{OCH}_2\text{CH}_2\text{O}$), 49.8 (C-1''), 25.7 (C– CH_3), 16.2 (C– CH_3), -5.4 (Si– Me_2); m/z 425 (29%, M^+ , ^{81}Br), 423 (29%, M^+ , ^{79}Br), 167 (35), 73 (100) (Found: M^+ (^{79}Br) 423.0886. $\text{C}_{19}\text{H}_{26}^{79}\text{BrNO}_3\text{Si}$ requires M 423.0865).

Radical cyclisations: general procedure

The amide in toluene was heated at 80 °C under argon. AIBN (0.1 equivalents) and tributyltin hydride were then added simultaneously, dropwise. AIBN (0.1 equivalents) was then added every hour for 3 hours. The reaction was then allowed to stir overnight at 80 °C. Toluene was removed *in vacuo*. The residue was dissolved in ethyl acetate and washed with 20% ammonia solution (5 × 100 ml). The organic layer was dried (MgSO_4) and the solvent removed *in vacuo*.

***N*-Methyl-3-*tert*-butyldimethylsilylmethylideneindol-2(3*H*)-one, 10a.** Amide **9a** (0.2 g, 0.57 mmol) and tributyltin hydride (0.17 ml, 0.63 mmol) gave **10a** as a mixture of *E*- and *Z*-isomers which were separable by chromatography (SiO_2 , 2% EtOAc–hexane).

Z-Isomer. A green solid (71 mg, 46%), mp 84–86 °C; R_f (30% EtOAc–hexane) 0.56; $\nu_{\max}/\text{cm}^{-1}$ 2925 (m, C–H), 1703 (s, C=O), 1611 (s, C=C), 1469 (s, benzene ring); δ_{H} (360 MHz; CDCl_3) 7.43 (1H, dd, J 7.5, 0.6, H-4), 7.27 (1H, td, J 7.5, 1.1, H-6), 7.03 (1H, s, H-1'), 7.01 (1H, td, J 7.5, 0.8, H-5), 6.76 (1H, d, J 7.5, H-7), 3.21 (3H, s, NMe), 1.00 (9H, s, $\text{C}(\text{CH}_3)_3$), 0.31 (6H, s, 2(CH_3)); δ_{C} (CDCl_3) 167.1 (C=O), 143.5 (C-7a), 142.3 (C-3a), 138.0 (C-4), 129.8 (C-6), 123.2 (C-3), 121.9 (C-5), 120.0 (C-1'), 107.9 (C-7), 26.5 (C– CH_3), 25.8 (N– CH_3), 17.1 (C– CH_3), -6.2 (Si– Me_2); m/z 273 (12.2%, M^+), 258 (52.3, $\text{M}^+ - \text{CH}_3$), 216 (100, $\text{M}^+ - \text{C}(\text{CH}_3)_3$), 201 (54.4), 186 (70.4), 158 (35) (Found: M^+ , 273.1541. $\text{C}_{16}\text{H}_{23}\text{NOSi}$ requires M 273.1549).

E-Isomer. A green solid (25 mg, 16%), R_f (30% EtOAc–hexane) 0.50; $\nu_{\max}/\text{cm}^{-1}$ 2929 (C–H), 1708 (s, C=O), 1611 (s, C=C), 1470 (s, benzene ring), 1265 (s, Si–C); δ_{H} (360 MHz; CDCl_3) 7.57 (1H, d, J 7.6, H-4), 7.30 (1H, s, H-1'), 7.29 (1H, t, J 7.6, H-6), 7.02 (1H, t, J 7.6, H-5), 6.81 (1H, d, J 7.6, H-7), 3.24 (3H, s, NMe), 1.01 (9H, s, $\text{C}(\text{CH}_3)_3$), 0.32 (6H, s, 2(CH_3)); δ_{C} (CDCl_3) 167.1 (C=O), 145.0 (C-7a), 141.8 (C-3a), 137.5 (C-4), 129.9 (C-6), 123.7 (C-3), 122.6 (C-1'), 121.8 (C-5), 108.5 (C-7), 29.7 (N–Me), 26.9 (C– CH_3), 17.4 (C– CH_3), -5.4 (Si– Me_2); m/z 273 (35.6%, M^+), 258 (13.9, $\text{M}^+ - \text{CH}_3$), 216 (85.6, $\text{M}^+ - \text{C}(\text{CH}_3)_3$), 201 (7.8), 186 (41.5), 158 (4.4), 28.0 (100) (Found: M^+ , 273.1544. $\text{C}_{16}\text{H}_{23}\text{NOSi}$ requires M 273.1549).

***N*-(Prop-2-enyl)-3-*tert*-butyldimethylsilylmethylideneindole-2(3*H*)-one, 10b.** Amide **9b** (0.9 g, 2.38 mmol) and tributyltin hydride (0.75 g, 2.61 mmol) gave **10b** as a mixture of *E*- and *Z*-isomers which were separable by chromatography (SiO_2 , 3% EtOAc–hexane).

Z-Isomer. A green oil (0.35 g, 49%), R_f (30% EtOAc–hexane) 0.56; $\nu_{\max}/\text{cm}^{-1}$ 2927 (m, C–H), 1705 (s, C=O), 1610 (s, C=C), 1470 (s, benzene ring); δ_{H} (360 MHz; CDCl_3) 7.45 (1H, dd, J 7.5,

0.7, H-4), 7.24 (1H, td, J 7.5, 1.2, H-6), 7.06 (1H, s, H-1'), 7.01 (1H, td, J 7.5, 1, H-5), 6.77 (1H, d, J 7.5, H-7), 5.85 (1H, m, H-2''), 5.21 (2H, m, H-3''), 4.36 (2H, dt, J 5.3, 1.7, H-1''), 1.00 (9H, s, $\text{SiC}(\text{CH}_3)_3$), 0.31 (6H, s, $\text{Si}(\text{CH}_3)_2$); δ_{C} (CDCl_3) 166.7 (C=O), 142.9 (C-7a), 142.2 (C-3a), 138.3 (C-4), 131.8 (C-2''), 129.7 (C-6), 123.4 (C-3), 121.9 (C-5), 120.1 (C-1'), 117.3 (C-1''), 108.8 (C-7), 42.1 (2C, CH_2 , C-3''), 26.5 ($\text{SiC}(\text{CH}_3)_3$), 17.2 ($\text{SiC}(\text{CH}_3)_3$), -6.1 ($\text{Si}(\text{CH}_3)_2$); m/z 299 (7.4%, M^+), 242 (100, $\text{M}^+ - \text{C}_4\text{H}_9$), 186 (75%) (Found: M^+ , 299.1695. $\text{C}_{18}\text{H}_{25}\text{NOSi}$ requires M 299.1705).

E-Isomer. A green oil (74 mg, 10%), R_f (30% EtOAc–hexane) 0.49; $\nu_{\max}/\text{cm}^{-1}$ 2927 (m, C–H), 1703 (s, C=O) 1610 (s, C=C), 1468 (s, benzene ring); δ_{H} (360 MHz; CDCl_3) 7.58 (1H, d, J 7.6, H-4), 7.31 (1H, s, H-1'), 7.25 (1H, td, J 7.6, 1.1, H-6), 7.01 (1H, td, J 7.6, 1, H-5), 6.81 (1H, d, J 7.6, H-7), 5.84 (1H, m, H-2''), 5.23 (2H, m, H-3''), 4.39 (2H, dt, J 5.2, 1.6, H-1''), 1.02 (9H, s, $\text{SiC}(\text{CH}_3)_3$), 0.33 (6H, s, $\text{Si}(\text{CH}_3)_2$); δ_{C} (CDCl_3) 166.0 (C=O), 148.0 (C-7a), 144 (C-3a), 137.8 (C-4), 131.6 (C-2''), 129.8 (C-6), 123.8 (C-1'), 122.5 (C-3), 121.8 (C-5), 117.5 (C-1''), 109.1 (C-7), 42.4 (2C, CH_2 , C-3''), 26.3 ($\text{SiC}(\text{CH}_3)_3$), 18.0 ($\text{SiC}(\text{CH}_3)_3$), -5.4 ($\text{Si}(\text{CH}_3)_2$); m/z 299 (9%, M^+), 242 (100, $\text{M}^+ - \text{C}_4\text{H}_9$) (Found: M^+ , 299.1697. $\text{C}_{18}\text{H}_{25}\text{NOSi}$ requires M 299.1705).

***N*-(1,3-Dioxolan-2-ylmethyl)-3-*tert*-butyldimethylsilylmethylideneindol-2(3*H*)-one, 15.** Amide **14** (1.7 g, 3.99 mmol) and tributyltin hydride (1.28 g, 4.38 mmol) gave **15** as a mixture of *E*- and *Z*-isomers separable by chromatography (SiO_2 , 3% EtOAc–hexane).

Z-Isomer. A green oil (0.62 g, 45%), R_f (30% EtOAc–hexane) 0.67; $\nu_{\max}/\text{cm}^{-1}$ 3054 (olefinic C–H), 2926 (C–H), 1652 (tertiary amide C=O), 1456 (benzene ring), 1265 (C–O); δ_{H} (360 MHz; CDCl_3) 7.43 (1H, d, J 7.6, H-4), 7.26 (1H, td, J 7.6, 1.0, H-6), 7.04 (1H, s, H-1'), 7.02 (1H, d, J 7.6, H-5), 6.99 (1H, t, J 7.6, H-7), 5.15 (1H, t, J 4.1, H-2''), 3.97 (2H, m, H-4'' or H-5''), 3.91 (2H, d, J 4.1, H-1''), 3.87 (2H, m, H-4'' or H-5''), 0.99 (9H, s, $\text{Si}(\text{CH}_3)_3$), 0.30 (6H, s, 2 × $\text{Si}(\text{CH}_3)_2$); δ_{C} (CDCl_3) 138.3 (C-4), 129.8 (C-6), 127.2 (C-3), 121.9 (C-5), 120.0 (C-1'), 109.3 (C-7), 101.9 (C-2''), 65.2 (CH_2), 42.9 (C-1''), 26.5 ($\text{SiC}(\text{CH}_3)_3$), 17.2 ($\text{SiC}(\text{CH}_3)_3$), -6.2 ($\text{Si}(\text{CH}_3)_2$); m/z 346 (33%, $\text{M}^+ + 1$), 345 (100, M^+), 288 (65, $\text{M}^+ - \text{C}_4\text{H}_9$) (Found: M^+ 345.1780. $\text{C}_{19}\text{H}_{27}\text{NO}_3\text{Si}$ requires M 345.1760).

E-Isomer. A green oil (0.3 g, 22%), R_f (30% EtOAc–hexane) 0.54; $\nu_{\max}/\text{cm}^{-1}$ 3054 (olefinic C–H), 2926 (C–H), 1652 (tertiary amide C=O), 1456 (benzene ring), 1265 (C–O); δ_{H} (360 MHz; CDCl_3) 7.56 (1H, d, J 7.3, H-4), 7.30 (1H, s, H-1'), 6.99–7.13 (3H, m, H-5, H-6, H-7), 5.13–5.17 (1H, m, H-2''), 3.97 (2H, m, H-4'' or H-5''), 3.95 (2H, d, J 4.1, H-1''), 3.87 (1H, m, H-4'' or H-5''), 1.01 (9H, s, $\text{Si}(\text{CH}_3)_3$), 0.32 (6H, s, 2 × $\text{Si}(\text{CH}_3)_2$); δ_{C} (CDCl_3) 166.8 (C=O), 144.4 (C-7a), 141.5 (C-3a), 137.7 (C-4), 129.8 (C-6), 128.0 (C-3), 123.6 (C-1'), 121.8 (C-5), 109.4 (C-7), 101.7 (C-2''), 65.1 (CH_2), 42.9 (C-1''), 26.4 ($\text{SiC}(\text{CH}_3)_3$), 17.3 ($\text{SiC}(\text{CH}_3)_3$), -5.4 ($\text{Si}(\text{CH}_3)_2$); m/z 345 (17.6%, M^+), 288 (100, $\text{M}^+ - \text{C}_4\text{H}_9$) (Found: M^+ 345.1783. $\text{C}_{19}\text{H}_{27}\text{NO}_3\text{Si}$ requires M 345.1760).

***N*-Methyl-3'-(*tert*-butyldimethylsilyl)spiro[indole-3,2'-oxiran]-2-one, 16a.** MCPBA (0.14 g, 50% w/v, 0.4 mmol) was added portionwise to a solution of **Z-10a** (0.1 g, 0.37 mmol) in dichloromethane (5 ml) at room temperature. The reaction mixture was stirred for 16 hours after which time a further quantity of MCPBA (0.14 g) was added. The reaction mixture was stirred for a further 2 hours and then sodium sulfite solution (10 ml, 10% w/v) was added to quench the reaction. The organic layer was washed with saturated sodium bicarbonate solution (3 × 5 ml), water (3 × 5 ml) and finally brine (3 × 5 ml). The organic layer was dried and evaporated under reduced pressure. Chromatography (SiO_2 , 15% EtOAc–hexane) gave the *title compound*, **16a** as a pale yellow oil (0.045 g, 43%); R_f (3:7 EtOAc–hexane) 0.52; $\nu_{\max}/\text{cm}^{-1}$ 2928 (C–H),

1709 (C=O), 1253 (epoxide C–O); δ_{H} (360 MHz; CDCl₃), 7.59 (1H, dd, *J* 7.5, 1.2, H-4), 7.29 (1H, td, *J* 7.5, 1.2, H-6), 7.09 (1H, t, *J* 7.5, H-5), 6.86 (1H, d, *J* 7.5, H-7), 3.27 (3H, s, NCH₃), 3.02 (1H, s, OCHSi), 0.65 (9H, s, Si(CH₃)₃), 0.41 (3H, s, SiCH₃), 0.18 (3H, s, SiCH₃); δ_{C} (CDCl₃) 172.31 (C=O), 141.55 (C-7a), 127.44 (C-4), 124.98 (C-6), 124.42 (C-3a), 122.38 (C-5), 107.9 (C-7), 66.74 (C-3), 61.1 (C-1'), 26.72 (SiC(CH₃)₃), 26.3 (NCH₃) 19.74 (SiC(CH₃)₃), –6.4 (SiCH₃), –6.6 (SiCH₃); *m/z* 289 (38.6%, M⁺), 232 (100, M⁺ – C₄H₉) (Found: M⁺ 289.1500. C₁₆H₂₃NO₂Si requires *M* 289.1498).

***N*-Prop-2-enyl-3'-(*tert*-butyldimethylsilyl)spiro[indole-3,2'-oxiran]-2-one, 16b.** Procedure as for **16a**. **Z-10b** (0.3 g, 1 mmol) gave the title compound, **16b** as a pale yellow oil (0.16 g, 51%) after chromatography (SiO₂, 15% EtOAc–hexane); *R_f*(3:7 EtOAc–hexane) 0.49; ν_{max} /cm^{–1} 1703 (C=O), 1610 (C=C), 1250 (epoxide C–O); δ_{H} (360 MHz; CDCl₃), 7.31 (1H, dd, *J* 7.7, 1.6, H-4), 7.11 (1H, td, *J* 7.7, 1.6, H-6), 7.05 (1H, t, *J* 7.7, H-5), 6.88 (1H, d, *J* 7.7, H-7), 5.84 (1H, m, CH=CH₂), 5.25 (1H, dd, *J* 11.8, 1, *cis*-C=CH₂), 5.22 (1H, dd, *J* 5.0, 1, *trans*-C=CH₂), 4.45 (1H, ddt, *J* 16.3, 5.2, 1, N-CH₂), 4.29 (1H, ddt, *J* 16.3, 5.3, 1, N-CH₂), 3.00 (1H, s, OCHSi), 0.99 (9H, s, Si(CH₃)₃), 0.36 (3H, s, SiCH₃), 0.08 (3H, s, SiCH₃); δ_{C} (CDCl₃) 172.5 (C=O), 143.9 (C-7a), 131.1 (C-4), 129.8 (C-6), 125.1 (C-3a), 122.7 (C-5), 121.7 (C-7), 117.7 (C=CH₂), 109.4 (C=CH₂), 60.8 (O-C-Si), 60.3 (C-3), 42.6 (N-CH₂), 26.4 (SiC(CH₃)₃), 17.0 (SiC(CH₃)₃), –7.05 (SiCH₃), –7.1 (SiCH₃); *m/z* 200 (30%, M⁺ – TBDMS), 73 (100). No M⁺ was observed and no HRMS could be determined.

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