

## Synthesis of pyrrolocarbazoles with *N*-substituted alkynyl-, alkylcyano- and alkylhydroxyl-groups

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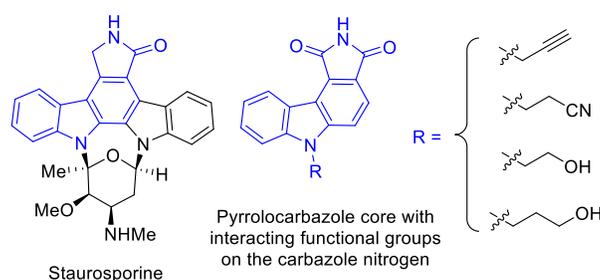
Received 11-03-2020

Accepted 11-28-2020

Published on line 12-07-2020

### Abstract

Due to their involvement in almost all stages of cellular life, kinase biomolecular catalysts have been linked to cancer development and, thus, remain attractive drug targets for cancer therapeutics. 6-(3'-Hydroxypropyl)-, 6-(2'-hydroxyethyl)-, 6-(2'-propynyl)- and 6-(3'-propanenitrile)-pyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-diones were synthesized as potential small molecule EGFR kinase inhibitors. The pyrrolocarbazole compounds were synthesized by way of a Diels-Alder approach involving *N*-alkylated 2-vinyl-1*H*-indole and maleimide as starting materials followed by aromatization with MnO<sub>2</sub>.



**Keywords:** Pyrrolocarbazole, kinase inhibitors, Diels-Alder, aromatization

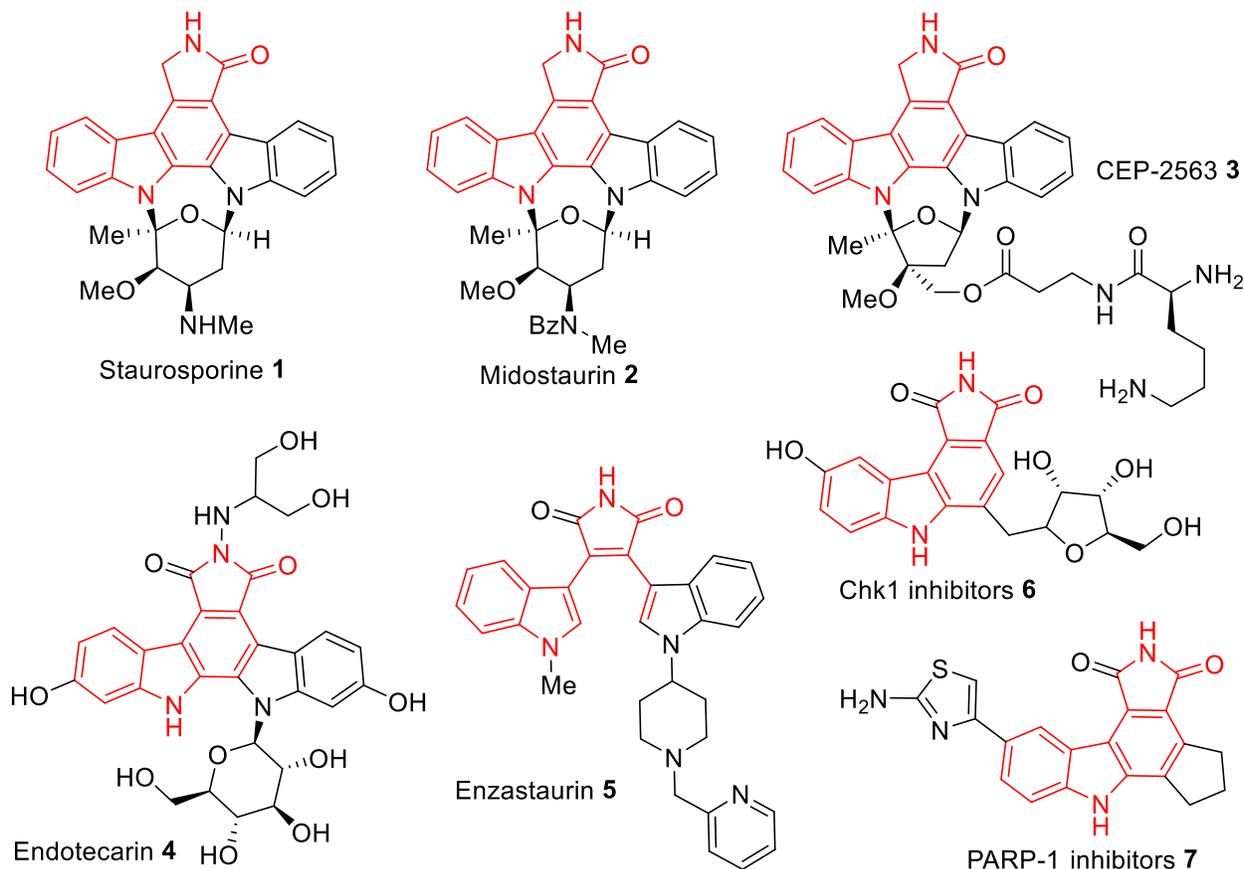
## Introduction

Over the past three decades, extensive research efforts have contributed to rapid developments in the field of oncology. Despite the apparent progress, cancer continues to be a worldwide leading cause of death. The need to develop new and less toxic treatments against a disease with the rather frustrating ability to remodel itself as drug-resistant variants is, thus, as important as ever.

The reversible phosphorylation of proteins is arguably one of the most general regulatory strategies adopted by eukaryotic cells and represents a key step in many crucial cellular processes. In this regard, protein kinases are enzymes that promote phosphorylation, i.e., the transfer of a phosphate group from ATP to a substrate protein. Due to the central involvement of kinases in almost all stages of cellular life (including growth factor signaling, cell cycle control, apoptosis and angiogenesis), these biocatalysts have been linked to cancer development and thus remain attractive drug targets for cancer therapeutics. The history concerning the development of kinase inhibitors has enjoyed much success; however, fundamental challenges, such as the lack of efficiency, drug resistance due to key amino acid mutations and inhibitor selectivity, persist. The development of effective long-term cancer treatments, including those which involve kinase inhibition, thus remains a pursuit of many researchers.

One of the most commonly selected kinase families targeted for the development of cancer therapeutics has been the receptor tyrosine kinases (RTKs), which include the epidermal growth factor receptors (EGFRs), the vascular endothelial growth factor receptors (VEGFRs) and the platelet-derived growth factor receptors (PDGFRs).<sup>1</sup> Many of these cell-surface receptors are known to be mutated or overexpressed in cancer systems, which makes them attractive candidates as targets. For this particular project, we decided to focus on the EGFR family which consists of EGFR, human EGRF-related 2 (HER2) and the kinase-impaired HER3 and HER4.<sup>2</sup> EGFR itself has been the target of many successful small-molecule drugs, including erlotinib, gefitinib, afatinib, the more recent osimertinib, and the more experimental brigatinib and icotinib. Even for the more recent compounds, the development of drug-resistant cancer cells is a serious limitation (see for instance, the exon 20 C797S mutation experienced by the 3<sup>rd</sup> generation inhibitor, osimertinib).<sup>3</sup>

In terms of finding inspiration for new scaffolds which might provide the basis for kinase inhibitors with different and, hopefully, favourable characteristics, Nature continues to be one of the best sources of ideas.<sup>4</sup> With this in mind, it was soon realized that staurosporine **1** is in fact a natural, potent kinase inhibitor, initially isolated from the bacterium *Streptomyces staurosporeus*, and has widely served as a structural muse for the design of protein kinase inhibitors with the overall aim of improved specificity and selectivity. Numerous staurosporine analogues have been evaluated against various human cancer cell lines, with some showing promising therapeutic activity.<sup>5-10</sup> Staurosporine-inspired drug candidates have been in vogue, see for instance the staurosporin-inspired midostaurin **2** (Rydapt<sup>®</sup>, in clinic as a tyrosine kinase 3 (FLT3) inhibitor), CEP-2563 **3** (phase 1) and endotecarin **4** (phase 3) depicted in Figure 1.<sup>10</sup> The bisaryl maleimide derivative enzastaurin **5** could be considered an “open” form of staurosporine, but, unfortunately, it failed its phase III lymphoma clinical trial. Structurally simplified staurosporine-inspired pyrrolocarbazoles have also been considered as possible kinase inhibitors – examples include Chk 1 inhibitors **6** and PARP 1 inhibitors **7** – and these simplified staurosporine motifs were the basis for the design of new potential inhibitors described in this work.



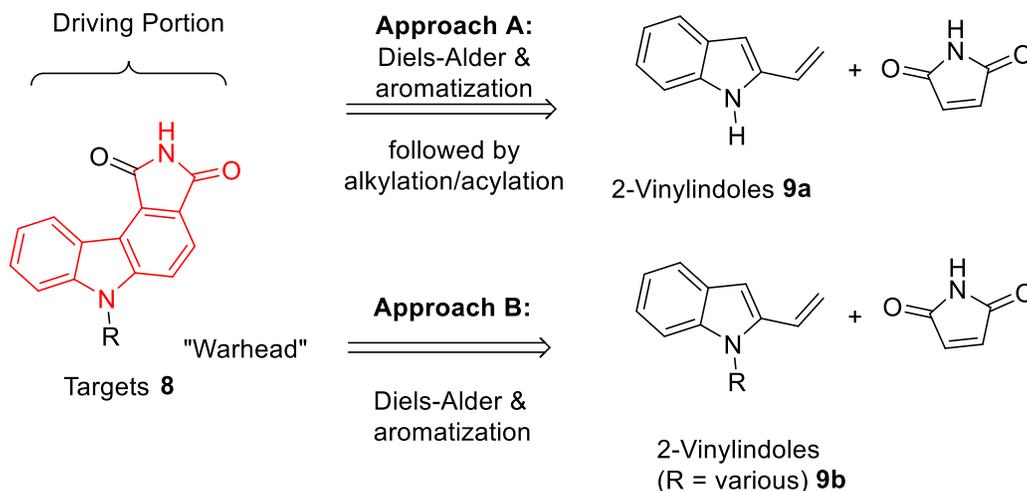
**Figure 1.** Staurosporine 1, and examples of other important indolo- and pyrrolocarbazoles (see following references for reviews on clinically relevant staurosporin analogues<sup>9</sup> and other relevant carbazoles<sup>10</sup>).

It should be noted that the pyrrolocarbazole core, apart from its ubiquitous role in natural products,<sup>11</sup> has seen frequent prior application in medicinal chemistry,<sup>12</sup> with particular emphasis as kinase inhibitors. Examples include earlier work focused on protein kinase C,<sup>13-14</sup> the checkpoint kinase Wee1<sup>15</sup> and Chk1<sup>16-20</sup>, mixed lineage kinase (MLK)<sup>21</sup> inhibitors, as well as other series with more generic anti-cancer applications.<sup>22-23</sup> Similar scaffolds have also been identified as PARP-1 inhibitors.<sup>24</sup>

In this project we envisaged the development of potential kinase inhibitors that would selectively suppress EGFR, an important therapeutic target (for other collaborative studies from our group involving this kinase see<sup>25-27</sup>). Exploiting the attractive features demonstrated by the natural product staurosporine, the design considered was based on a staurosporine scaffold. It was our intention that the pyrrolocarbazole scaffold **8** could act as a driving portion and present a suitable platform to incorporate potentially electrophilic warheads (R) at a proper trajectory (Figure 2). Notably, the scaffold displaying the warhead at a particular distance and orientation, could result in a covalent interaction to cysteine 797 in the kinase-active site, a strategy utilized before in our research.<sup>26,28</sup>

In terms of the synthetic strategy towards the desired substituted scaffolds, a Diels-Alder-oxidative aromatization approach was utilized. (For an excellent overview of the many synthetic approaches to the carbazole scaffold, please refer to the review by Knölker and co-workers<sup>11</sup>). Approach A involved generating the pyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione first, followed by selective acylation/alkylation of the carbazole nitrogen atom as shown in Figure 2. Alternatively, approach B would generate the desired compounds with the desired N-functionalizations already in place on the 2-vinylindole precursor **9b**. It should be noted that the

Diels-Alder/aromatization strategy has been effectively utilized before to efficiently deliver substituted pyrrolocarbazoles (see the examples listed in the following references<sup>13-15,17-18,21-22,24</sup> and the following examples which include related modifications<sup>29-32</sup> with respect to the 2-vinylindole motif<sup>33</sup>).

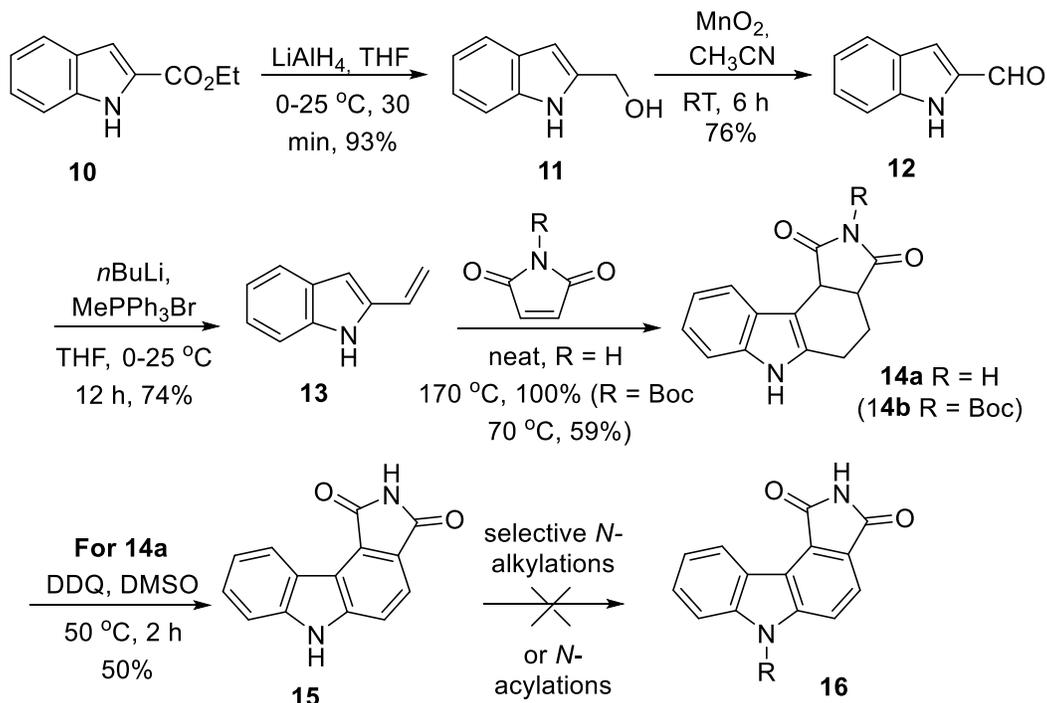


**Figure 2.** Retrosynthetic analysis to afford pyrrolocarbazole skeletons **8** containing a group on the nitrogen atom of the resultant carbazole (Route B was eventually the successful one).

## Results and Discussion

The initial strategy focused on the synthesis of the known pyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione scaffold **15** in order to use this compound in a divergent approach to obtain a small library of alkylated *N*-carbazole derivatives. To this end, commercially available ethyl 1*H*-indole-2-carboxylate **10** was converted into 1*H*-indole-2-carbaldehyde **12**, via alcohol **11**, through a reduction (LiAlH<sub>4</sub>)-oxidation (MnO<sub>2</sub>) sequence. A Wittig reaction (MePPh<sub>3</sub>Br with *n*BuLi) involving carbaldehyde **12** readily afforded 2-vinyl-1*H*-indole **13**, which gratifyingly underwent a Diels-Alder reaction as a neat mixture at 170 °C with maleimide to afford the fused indole **14a** in quantitative yield. This compound was then oxidized into the fully-aromatized substituted carbazole scaffold **15** with DDQ in DMSO at 50 °C in 50% yield (Scheme 1).

Initial attempts to react **15** with acryloyl chloride in DMF at 0 °C to obtain *N*-acylated **16**, and even after heating to 80 °C under N<sub>2</sub> for 48 h, did not indicate any evidence of *N*-substituted product **16** formation by TLC. In addition, treatment of **15** with NaH in DMF at RT under N<sub>2</sub> afforded a purple solution which turned a yellow color upon the drop-wise addition of acryloyl chloride with stirring at RT for 4 days, but still gave no new products (TLC). To address the regioselectivity issue between the two nitrogen atoms in **15**, the known *N*-Boc-protected maleimide<sup>34</sup> was reacted with diene **13** at 70 °C for 30 min to afford the expected adduct **14b** in 59% yield. Attempts to react this latter adduct with acryloyl chloride, in DMF containing DIPEA (-5 to 60 °C for 2 days), only led to the cleavage of the Boc-protecting group. Aromatization of **14b** with either DDQ or MnO<sub>2</sub> also resulted in the Boc group being cleaved. The unsuccessful work involving the Boc-protected compounds is not described further.

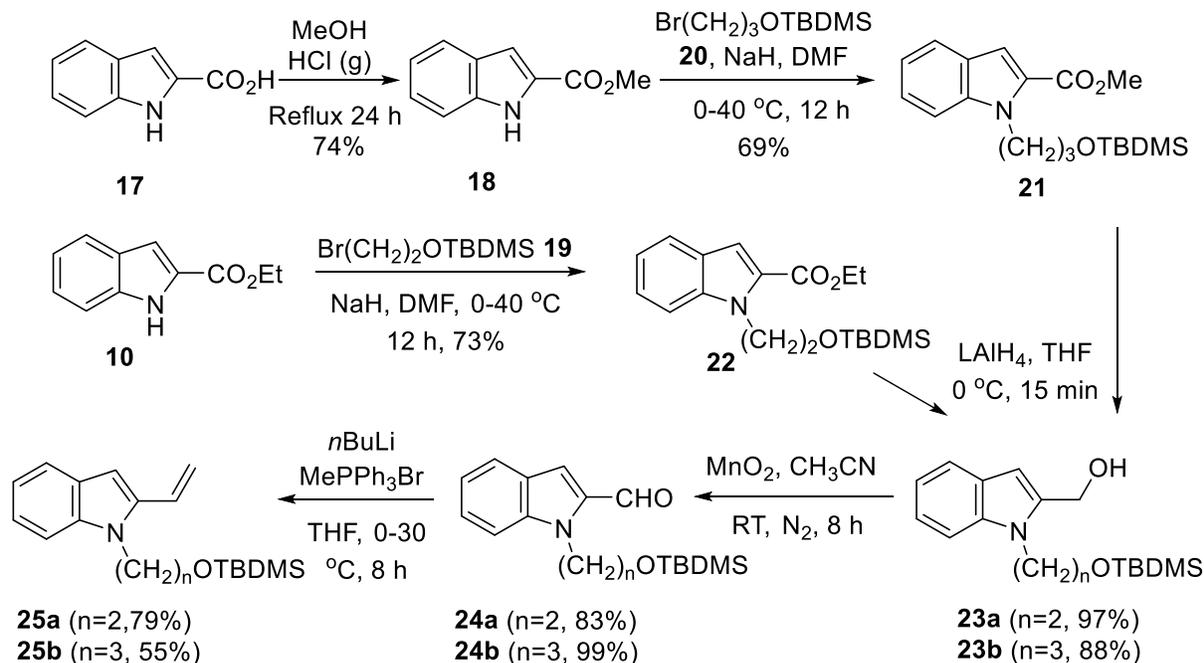


**Scheme 1.** Synthesis of pyrrolocarbazole dione **15** and attempted unsuccessful maleimide acylation/alkylations.

An alternative method at accessing N-substituted carbazoles involved the initial introduction of substituents on the nitrogen atom of the indole ring by the synthesis of N-alkylated 2-vinylindoles. These could, subsequently, be utilized as the starter dienes in the critical Diels-Alder cyclization step. To this end, ethyl and methyl 1H-indole-2-carboxylates **10** and **18**, respectively (the latter readily obtained from carboxylic acid **17**), were dissolved in DMF to which NaH was added, followed by (2-bromoethoxy)(*tert*-butyl)dimethylsilane (**19**)<sup>35</sup> or (3-bromopropoxy)(*tert*-butyl)dimethylsilane (**20**)<sup>36</sup> to afford **22** and **21**, respectively, in reasonable yields (Scheme 2). Reduction of **22** and **21** was readily achieved by the use of  $\text{LiAlH}_4$  in THF at 0 °C to afford **23a** and **23b** in excellent yields of 97% and 88%, respectively. It should be noted, however, that the reaction temperature needed to remain below room temperature in order to retain the ethoxy and propoxy silyl groups; at temperatures above room temperature these groups were cleaved.

$\text{MnO}_2$  was found to be the best oxidizing agent for the conversion of **23a** and **23b** into substituted 1H-indole-2-carbaldehydes **24a** and **24b** in respectable yields of 83% and 99%, respectively. Prior activation of the  $\text{MnO}_2$  was necessary and achieved by placing a beaker of  $\text{MnO}_2$  in an oven at 120 °C for 24 h. The oxidant, after the oxidation procedure, was readily removed by filtration and it was found that the aldehyde products were sufficiently pure to be used for conversion into the respective vinyl analogues without further chromatographic purification.

The Wittig protocol for conversion of the aldehydes into their corresponding vinyl analogues involved the initial generation of the methylene ylide, by treatment of  $\text{MePPh}_3\text{Br}$  with  $n\text{BuLi}$  in dry THF at 0 °C, followed by the drop-wise addition of carbaldehydes **24a** and **24b** to afford the two alkylated 2-vinyl-1H-indoles **25a** and **25b** in yields of 79% and 55% respectively.

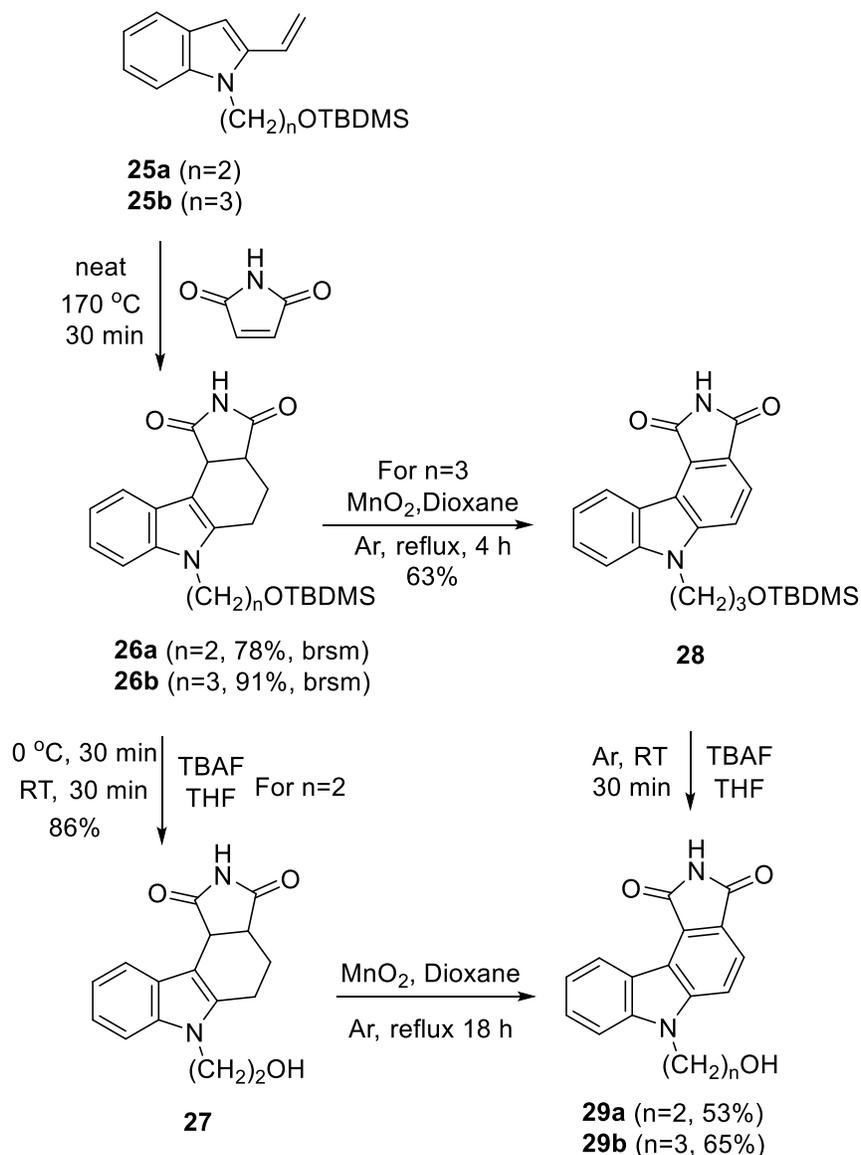


**Scheme 2.** Synthesis of *N*-alkylated 2-vinylindoles **25a** and **25b**.

The key Diels-Alder reaction to produce the additional 6-membered ring of the desired pyrrolocarbazole scaffold involved the cycloaddition of compounds **25a** and **25b** with maleimide. The reagents were heated together as a neat mixture and, after melting, they reacted to produce a solid adduct, which, in both cases, was purified chromatographically to afford the desired products **26a** and **26b** in reasonable yields of 78% and 91%, respectively, based on recovered starting material (brsm) (Scheme 3).

The target pyrrolocarbazoles **29a** and **29b** were prepared by a protocol involving the same steps, but in the opposite order, since it was found that this alternative sequence produced the best overall yields. Thus for pyrrolocarbazole **29a**, adduct **26a** was firstly treated with TBAF at 0 °C to remove the TBDMS protecting group to produce **27** in 86% yield, followed by the MnO<sub>2</sub> oxidation in dioxane under reflux to form the desired aromatized product **29a** in a yield of 53%. On the other hand, **29b** was readily obtained by first oxidizing **26b** with MnO<sub>2</sub> in refluxing dioxane to form the aromatized carbazole **28** in 63% yield, followed by cleavage of the TBDMS protecting group with TBAF in THF at RT for 30 min, to afford the longer chain product **29b** in 65% yield.

The propargyl group was introduced on the nitrogen atom of the previously synthesized 2-vinyl-1*H*-indole (**13**) by a nucleophilic substitution reaction employing Cs<sub>2</sub>CO<sub>3</sub> as a base, as per a literature procedure,<sup>37</sup> to afford **30a** in a moderate (45%) yield. We found the best way to introduce the cyanoethyl group on the nitrogen atom of indole **13**, in order to obtain **30b**, involved a Michael addition between the 2-vinyl-1*H*-indole (**13**) and acrylonitrile in the presence of DBU in acetonitrile, at RT for 8 h, which gave the desired product **30b** in 84% yield [based on recovered starting material (brsm)], as shown in Scheme 4.

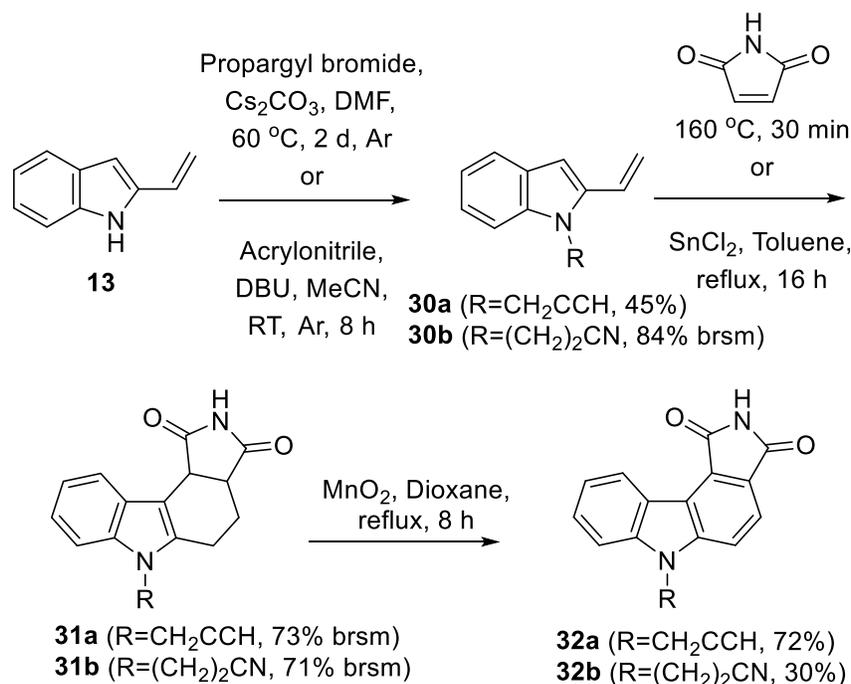


**Scheme 3.** Synthesis of the *N*-alkylated pyrrolocarbazoles **29a** and **29b**.

A Diels-Alder reaction between compound **30a** and maleimide was successfully achieved in the same manner as described previously, but at a slightly lower reaction temperature of  $160\text{ }^\circ\text{C}$ . It should be noted that cycloadduct **31a** was obtained in an acceptable yield of 73% (brsm) and, thus, in sufficient amounts to carry on with the syntheses. For the cycloaddition between diene **30b** and maleimide, it was found that the addition of a Lewis acid,  $\text{SnCl}_2$ , produced the best results. Even under the best conditions available, however, unreacted starting material was still present which, fortunately, could easily be separated by chromatography. In this latter case, the cycloadduct **31b** was obtained in an acceptable yield of 71% (calculated brsm).

Finally, aromatization of the cyclohexene ring of **31a** and **31b**, using an excess of  $\text{MnO}_2$  in refluxing dioxane, afforded the desired substituted pyrrolocarbazoles **32a** and **32b** in yields of 72% and 30%, respectively. It should be noted that pyrrolocarbazoles **32a** and **32b** were found to be quite insoluble in most laboratory solvents which precluded their absolute purification by chromatography. Consequently, a trituration protocol for **32a** and a recrystallization from DMF for **32b** were employed to obtain the final

compounds in sufficient purity. The recrystallization from DMF, unfortunately, afforded **32b** in a rather low yield.



**Scheme 4.** Synthesis of pyrrolocarbazoles **32a** and **32b**.

Initial biochemical evaluations on substituted pyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-diones **29a,b** and **32a,b** were, unfortunately, underwhelming. These compounds were, thus, added to a small-molecule kinase library, and could represent starting points for future screening initiatives.

## Conclusions

A set of four carbazole N-substituted pyrrolocarbazoles bearing the 6-(3'-hydroxypropyl)-, 6-(2'-hydroxyethyl)-, 6-(2'-propynyl)- and 6-(3'-propanenitrile)-fragments on their nitrogen atoms was prepared for evaluation as potential EGFR kinase inhibitors using Diels Alder cycloadditions and  $\text{MnO}_2$  oxidative aromatizations to good effect. These compounds will be utilized as part of screening libraries for the identification of potential lead compounds in future high-throughput screenings.

## Experimental Section

**General.** Purification of solvents and reagents: Ethyl acetate and hexane used for chromatographic purposes were distilled by means of conventional distillation procedures. Solvents used for reaction purposes were dried over an appropriate drying agent and distilled under nitrogen gas. Tetrahydrofuran, 1,4-dioxane, and diethyl ether were distilled from sodium wire using benzophenone as an indicator. Dimethylformamide and acetonitrile were distilled from calcium hydride.

Chromatography: Separation of compounds by column chromatography was performed using Merck silica gel (particle size 0.063–0.200 mm). Thin layer chromatography was performed using Merck silica gel 60 F<sub>254</sub> coated on aluminium sheets. Compounds on TLC plates were viewed under UV light.

Spectroscopic and physical data: <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker ADVANCE 300 or Varian Gemini-300 spectrometer (<sup>1</sup>H NMR at 300 MHz and <sup>13</sup>C at 75 MHz). A Varian VXR-400 machine (<sup>1</sup>H NMR at 400 MHz and <sup>13</sup>C NMR at 101 MHz) or 600 MHz Varian Unity Inova (<sup>1</sup>H NMR at 600 MHz and <sup>13</sup>C NMR at 151 MHz) were also utilized. Spectra were recorded in deuterated chloroform (CDCl<sub>3</sub>) and DMSO (DMSO-*d*<sub>6</sub>) as indicated. Infra-red spectra were recorded using a Bruker Tensor 27 spectrometer. Melting points were measured using a Stuart SMP10 melting point machine. Mass spectra were recorded on a Thermo Electron DFS Magnetic Sector Mass Spectrometer (E.I. mode).

Other general procedures: Most reactions were carried out under nitrogen or argon and reaction vessels were dried in an oven. Removal of solvent *in vacuo* refers to removal of the solvent using a rotary evaporator followed by removal of trace amounts of solvent using a high vacuum pump.

**(1*H*-Indol-2-yl)methanol (11).** LiAlH<sub>4</sub> (0.88 g, 23 mmol, 2.2 equiv.) was stirred in THF (10 mL) in a 250 mL two-neck round-bottom flask at 0 °C under N<sub>2</sub>. A solution of commercially available ethyl indole-2-carboxylate (**10**) (2.0 g, 10 mmol) in THF (10 mL) was then added drop-wise to the LiAlH<sub>4</sub> solution. The ice bath was removed and the reaction mixture warmed to 25 °C and stirred for 30 min. After cooling to 0 °C, H<sub>2</sub>O (2 mL) was added drop-wise, followed by NaOH (1 M, aq., 5 mL) and again H<sub>2</sub>O (6 mL) and the reaction mixture was stirred for 30 min at RT. The solution was filtered through Celite and washed with CH<sub>2</sub>Cl<sub>2</sub> (100 mL). The filtrate was washed with brine (100 mL) and the organic layer, after drying (MgSO<sub>4</sub>) gave a residue which was purified by column chromatography (EtOAc/Hexane, 1:4) to afford **11** as an off-white solid (1.4 g, 93%) whose <sup>1</sup>H NMR spectrum compared very well to the literature.<sup>38</sup> <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 8.36 (s, 1H, NH), 7.59 (dd, *J* 7.9, 0.8 Hz, 1H, ArH), 7.33 (dd, *J* 8.1, 0.8 Hz, 1H, ArH), 7.19 (ddd, *J* 8.1, 7.1, 1.2 Hz, 1H, ArH), 7.14 – 7.08 (m, 1H, ArH), 6.40 (dd, *J* 2.0, 0.8 Hz, 1H, H-3), 4.80 (s, 2H, OCH<sub>2</sub>), 1.99 (s, 1H, OH); R<sub>f</sub> = 0.39 (EtOAc/Hexane, 4:6).

**1*H*-Indole-2-carbaldehyde (12).** MnO<sub>2</sub> (8.41 g, 96.8 mmol, 10 equiv.) was added to a solution of **11** (1.42 g, 9.68 mmol) in freshly distilled MeCN (90 mL) and the mixture stirred at RT for 6 h. The MnO<sub>2</sub> was then removed by filtration through Celite, followed by rinsing with EtOAc (50 mL) to afford an orange filtrate. Removal of the solvent afforded **12** as a yellow/orange solid (1.1 g, 76%) the <sup>1</sup>H NMR spectrum of which corresponded to the literature.<sup>35,38</sup> <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 9.86 (s, 1H, CHO), 9.36 (s, 1H, NH), 7.77 (ddd, *J* 8.1, 1.5, 0.9 Hz, 1H, ArH), 7.48 (dd, *J* 8.4, 1.2 Hz, 1H, ArH), 7.40 (ddd, *J* 8.4, 6.8, 1.5 Hz, 1H, ArH), 7.29 (dd, *J* 2.1, 0.9 Hz, 1H, H-3), 7.19 (ddd, *J* 8.1, 6.8, 1.2 Hz, 1H, ArH); R<sub>f</sub> = 0.77 (EtOAc/Hexane, 2:3).

**2-Vinyl-1*H*-indole (13).** Methyltriphenylphosphonium bromide (MePPh<sub>3</sub>Br) (7.39 g, 20.7 mmol, 6 equiv.) and dry THF (140 mL) were added to a two-neck round-bottom flask under N<sub>2</sub> in an ice bath and *n*BuLi (13.5 mL, 19.0 mmol, 5.5 equiv.) was added drop-wise to the solution at 0 °C. During this time, the color of the solution changed from white to a deep yellow. The ice bath was removed and the temperature increased to 30 °C. The solution was stirred for 30 min at this temperature and then cooled to 0 °C. Carbaldehyde **12** (0.500 g, 3.45 mmol) in THF (20 mL) was then added drop-wise to the methylenetriphenylphosphorane solution at 0 °C. The ice bath was removed and the mixture stirred overnight at RT under N<sub>2</sub> after which diethylether (80 mL) was added and the reaction mixture was washed with H<sub>2</sub>O (2 × 80 mL). The aqueous layer was collected and further extracted with Et<sub>2</sub>O (2 × 50 mL). The organic layers were combined, washed with brine (200 mL), dried (MgSO<sub>4</sub>) and the residue purified by chromatography (EtOAc/Hexane, 5:95) to afford **13** as an off-white solid (0.361 g, 74%), the <sup>1</sup>H NMR spectrum of which compared well to that in the literature.<sup>35</sup> <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.15 (s, 1H, NH), 7.58 (ddd, *J* 8.2, 1.1, 0.9 Hz, 1H, ArH), 7.33 (ddd, *J* 8.1, 1.5, 0.9 Hz, 1H, ArH), 7.19

(ddd,  $J$  8.2, 7.1, 1.5 Hz, 1H, ArH), 7.09 (ddd,  $J$  8.1, 7.1, 1.1 Hz, 1H, ArH), 6.75 (dd,  $J$  17.8, 11.2 Hz, 1H, H-1'), 6.53 (d,  $J$  2.1 Hz, 1H, H-3), 5.55 (d,  $J$  17.8 Hz, 1H, *trans* H-2'), 5.27 (d,  $J$  11.2 Hz, 1H, *cis* H-2');  $R_f$  = 0.47 (EtOAc/Hexane, 1:9).

**4,5,6,10c-Tetrahydropyrrolo[3,4-*c*]carbazole-1,3(2H,3aH)-dione (14a).** A neat mixture of indole **13** (0.500 g, 3.50 mmol) and maleimide (0.407 g, 4.19 mmol, 1.2 equiv.) in a round-bottom flask (5 mL) was placed in an oil bath preheated to 170 °C and kept at this temperature for 1 h to form **14a** as a brown, highly insoluble, solid (0.840 g, 100%) which was used without further purification. mp = 160 – 162 °C;  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ )  $\delta$  10.95 (s, 1H, NH), 7.70 (d,  $J$  7.2 Hz, 1H, ArH), 7.26 (d,  $J$  7.4 Hz, 1H, ArH), 7.07 – 6.93 (m, 2H, ArH), 4.17 (d,  $J$  8.1 Hz, 1H, H-10c), 3.50 – 3.42 (m, 1H, H-5/6), 3.17 (d,  $J$  5.1 Hz, 1H, H-4), 2.77 – 2.66 (m, 1H, H-5/6), 2.33 – 2.22 (m, 1H, H-5/6), 1.88 – 1.73 (m, 1H, H-5/6); IR (ATR,  $\text{cm}^{-1}$ ) 3382, 3222, 2961, 2943, 1703, 756, 745. HRMS calcd for  $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}_2^+$  [M+H] $^+$ , 241.0977, found 241.0966;  $R_f$  = 0.22 (MeOH/EtOAc/Hexane, 1:1:3).

**Pyrrolo[3,4-*c*]carbazole-1,3(2H,6H)-dione (15).** To a stirred solution of dione **14a** (0.150 g, 0.630 mmol) in DMSO (7 mL) at 30 °C under  $\text{N}_2$  was added DDQ (0.286 g, 1.26 mmol, 2 equiv.) after which the temperature was increased to 50 °C and stirring continued for 2 h. Water (10 mL) was then added drop-wise to form a precipitate which was filtered off and washed with  $\text{Et}_2\text{O}$  and dried under high vacuum to afford the aromatised product **15** as a brown solid (0.074 g, 50%). mp = 250 – 252 °C;  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ )  $\delta$  12.08 (s, 1H, NH), 11.12 (s, 1H, NH), 8.82 (d,  $J$  8.0 Hz, 1H, ArH), 7.85 (d,  $J$  8.2 Hz, 1H, ArH), 7.79 (d,  $J$  8.2 Hz, 1H, ArH), 7.65 – 7.52 (m, 2H, ArH), 7.32 (ddd,  $J$  8.2, 6.8, 1.3 Hz, 1H, ArH);  $^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ )  $\delta$  170.4 (CO), 170.3 (CO), 144.1 (ArC), 141.5 (ArC), 128.1 (ArC), 126.7 (ArCH), 124.7 (ArCH), 123.8 (ArC), 120.1 (ArCH), 120.0 (ArC), 119.42 (ArCH), 118.3 (ArC), 115.6 (ArCH), 111.6 (ArCH); IR (ATR,  $\text{cm}^{-1}$ ) 3186, 3057, 1697, 1451, 740; HRMS calcd for  $\text{C}_{14}\text{H}_9\text{N}_2\text{O}_2^+$  [M+H] $^+$ , 237.0664, found 237.0659;  $R_f$  = 0.84 (EtOAc).

**Methyl 1H-indole-2-carboxylate (18).** Into a two-neck round-bottom flask fitted with a condenser was placed methanol (130 mL) followed by commercially-available indole-2-carboxylic acid **17** (5.00 g, 31.0 mmol). The solution was saturated with HCl gas followed by heating under reflux for 24 h. The reaction mixture was treated with saturated aqueous sodium bicarbonate until effervescence ceased, concentrated in vacuo, and the residue extracted with EtOAc (3  $\times$  100 mL). The organic phases were combined and washed with brine. Hexane was added until a slight cloudiness persisted, and the solution was cooled in an ice bath to precipitate **18** as a white powder (4.04 g, 74%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  9.33 (s, 1H, NH), 7.69 (d,  $J$  8.1 Hz, 1H, ArH), 7.42 (d,  $J$  8.3 Hz, 1H, ArH), 7.31 (app. t, dd,  $J$  7.6 Hz, 1H, ArH), 7.23 (s, 1H, ArH), 7.14 (app. t, dd,  $J$  7.5 Hz, 1H, ArH), 3.95 (s, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  162.8 (CO), 137.1 (ArC), 127.5 (ArC), 127.1 (ArC), 125.4 (ArCH), 122.7 (ArCH), 120.8 (ArCH), 112.0 (ArCH), 108.9 (ArCH), 52.1 ( $\text{CH}_3$ ); IR (ATR,  $\text{cm}^{-1}$ ) 3332, 1689, 1527, 1438, 1255; HRMS calcd for  $\text{C}_{10}\text{H}_{10}\text{NO}_2$  [M+H] $^+$ , 176.0712, found 176.0657;  $R_f$  = 0.32 (20% EtOAc/Hexane).

**Ethyl 1-[2'-(*tert*-butyldimethylsilyloxy)ethyl]-1H-indole-2-carboxylate (22).** To a dry, two-neck round-bottom flask charged with commercially available ethyl indole-2-carboxylate **10** (1.5 g, 7.9 mmol) under argon was added dry DMF (10 mL) and the solution cooled to 0 °C in an ice bath. NaH (0.37 g, 9.5 mmol, 1.2 equiv.) was added in portions at 0 °C and the final mixture stirred for 10 min. (2-Bromoethoxy)(*tert*-butyl)dimethylsilane **19**<sup>36</sup> (2.1 g, 8.7 mmol, 1.1 equiv.) in DMF (5 mL) was then added drop-wise to the reaction mixture and stirred at 40 °C, under  $\text{N}_2$ , overnight. The reaction mixture was cooled to RT, poured onto cold (5 °C)  $\text{H}_2\text{O}$  (50 mL) and extracted with EtOAc (50 mL). The organic layer was then washed with brine (80 mL), dried ( $\text{MgSO}_4$ ), and the residue obtained was purified by chromatography (EtOAc/Hexane, 5:95) affording **22** as a clear liquid (0.27 g, 73%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.60 (d,  $J$  7.9 Hz, 1H, ArH), 7.44 (d,  $J$  8.3 Hz, 1H, ArH), 7.22 – 7.28 (m, 2H, ArH), 7.08 (dd,  $J$  10.9, 3.9 Hz, 1H, ArH), 4.64 (t,  $J$  5.4 Hz, 2H,  $\text{OCH}_2$ ), 4.32 (q,  $J$  7.2 Hz, 2H,  $\text{CH}_2$ ), 3.89 (t,  $J$  5.4 Hz, 2H,  $\text{NCH}_2$ ), 1.36 (t,  $J$  7.2 Hz, 3H,  $\text{CH}_2\text{CH}_3$ ), 0.70 (s, 9H, 3  $\times$   $\text{CH}_3$ ), -0.26 (s, 6H, 2  $\times$   $\text{CH}_3$ );  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  162.3 (CO), 140.2 (ArC), 127.7 (ArC), 126.0 (ArC), 124.9 (ArCH), 122.5 (ArCH), 120.6 (ArCH), 111.5 (ArCH), 110.8

(ArCH), 63.2 (OCH<sub>2</sub>), 60.6 (OCH<sub>2</sub>), 47.0 (NCH<sub>2</sub>), 25.9 (3 x CH<sub>3</sub>), 18.3 (C(CH<sub>3</sub>)<sub>3</sub>), 14.5 (CH<sub>3</sub>), -5.6 (2 x CH<sub>3</sub>); IR (ATR, cm<sup>-1</sup>) 2957, 2929, 2857, 1708, 1358, 1252, 1220, 1196, 1080; HRMS calcd for C<sub>19</sub>H<sub>30</sub>NO<sub>3</sub>Si<sup>+</sup> [M+H]<sup>+</sup>, 348.1995, found 348.2007; R<sub>f</sub> = 0.88 (EtOAc/Hexane, 2:8).

**Methyl 1-[3'-(*tert*-butyldimethylsilyloxy)propyl]-1*H*-indole-2-carboxylate (21).** Carboxylate **21** was synthesized in a similar manner to **22** using indole **18** (2.00 g, 11.4 mmol), sodium hydride (0.597 g, 14.8 mmol) and silyl compound **20** (3.22 g, 12.7 mmol)<sup>39</sup> to provide indole **21** as a clear oil (2.73 g, 69%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.66 (d, *J* 8.0 Hz, 1H, ArH), 7.51 (d, *J* 8.4 Hz, 1H, ArH), 7.35 – 7.30 (m, 2H, ArH), 7.14 (app. t, dd, *J* 7.4 Hz, 1H, ArH), 4.66 (t, *J* 7.1 Hz, 2H, OCH<sub>2</sub>), 3.90 (s, 3H, CH<sub>3</sub>), 3.63 (t, *J* 5.8 Hz, 2H, NCH<sub>2</sub>), 2.06 – 1.95 (m, 2H, CH<sub>2</sub>), 0.94 (s, 9H, 3 x CH<sub>3</sub>), 0.06 (s, 6H, 2 x CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 162.4 (CO), 139.4 (ArC), 127.0 (ArC), 125.8 (ArC), 124.9 (ArCH), 122.5 (ArCH), 120.5 (ArCH), 110.8 (ArCH), 110.6 (ArCH), 60.2 (OCH<sub>2</sub>), 51.6 (OCH<sub>3</sub>), 41.7 (NCH<sub>2</sub>), 33.8 (CH<sub>2</sub>), 25.9 (3 x CH<sub>3</sub>), 18.3 (C(CH<sub>3</sub>)<sub>3</sub>), -5.4 (2 x CH<sub>3</sub>); IR (ATR, cm<sup>-1</sup>) 2953, 1713, 1463, 1246, 1192, 1140; HRMS calcd for C<sub>19</sub>H<sub>29</sub>NO<sub>3</sub>Si [M<sup>+</sup>], 347.1917, found 347.1913; R<sub>f</sub> = 0.13 (2% EtOAc/Hexane).

**{1-[2'-(*tert*-Butyldimethylsilyloxy)ethyl]-1*H*-indol-2-yl}methanol (23a).** To a stirred slurry of LiAlH<sub>4</sub> (0.22 g, 5.8 mmol, 2 equiv.) in dry THF (10 mL) in a two-neck round-bottom flask under argon was added a solution of **22** (1.0 g, 2.9 mmol) in dry THF (10 mL) drop-wise at 0 °C. The reaction mixture was stirred for 15 min at 0 °C after which H<sub>2</sub>O (2 mL), NaOH (1 M, aq., 5 mL) and more H<sub>2</sub>O (6 mL) were successively added drop-wise and stirring continued at RT for 30 min. Filtration of the reaction mixture through Celite was followed by washing the filter plug with CH<sub>2</sub>Cl<sub>2</sub> (50 mL). The filtrate was washed with brine (50 mL) and the organic layer was dried (MgSO<sub>4</sub>) and the residue was purified by chromatography (EtOAc/Hexane, 2:8) affording **23a** as a white solid (0.85 g, 97%).

Mp 66 – 68 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.61 (d, *J* 7.8 Hz, 1H, ArH), 7.40 (d, *J* 8.0 Hz, 1H, ArH), 7.30 – 7.27 (m, 1H, ArH), 7.24 – 7.18 (m, 1H, ArH), 6.48 (s, 1H, ArH), 4.78 (s, 2H, OCH<sub>2</sub>), 4.37 (t, *J* 5.2 Hz, 2H, OCH<sub>2</sub>), 4.00 (t, *J* 5.2 Hz, 2H, NCH<sub>2</sub>), 3.23 (s, 1H, OH), 0.78 (s, 9H, 3 x CH<sub>3</sub>), -0.13 (d, *J* 3.0 Hz, 6H, 2 x CH<sub>3</sub>); <sup>13</sup>C NMR (105 MHz, CDCl<sub>3</sub>) δ 139.7 (ArC), 137.0 (ArC), 127.9 (ArC), 121.9 (ArCH), 121.2 (ArCH), 119.8 (ArCH), 109.5 (ArCH), 101.8 (ArCH), 62.2 (OCH<sub>2</sub>), 57.0 (OCH<sub>2</sub>), 45.7 (NCH<sub>2</sub>), 25.9 (3 x CH<sub>3</sub>), 18.5 (C(CH<sub>3</sub>)<sub>3</sub>), -5.7 (2 x CH<sub>3</sub>). HRMS calcd for C<sub>17</sub>H<sub>28</sub>NO<sub>2</sub>Si<sup>+</sup> [M+H]<sup>+</sup>, 306.1889, found 306.1889; IR (ATR, cm<sup>-1</sup>): 3258, 2926, 2854, 1251, 1111; R<sub>f</sub> = 0.84 (EtOAc/Hexane, 4:6)

**{1-[3'-(*tert*-Butyldimethylsilyloxy)propyl]-1*H*-indol-2-yl}methanol (23b).** The compound **23b** was synthesized in a similar manner to **23a** making use of the following reagents: **21** (2.18 g, 6.28 mmol) and LiAlH<sub>4</sub> (0.238 g, 6.28 mmol) to produce alcohol **23b** as a green-colored oil (1.77 g, 88%), which required no further purification and was used directly in the next reaction. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.58 (d, *J* 7.8 Hz, 1H, ArH), 7.35 (d, *J* 8.2 Hz, 1H, ArH), 7.20 (app. t, dd, *J* 7.6 Hz, 1H, ArH), 7.09 (app. t, dd, *J* 7.4 Hz, 1H, ArH), 6.45 (s, 1H, ArH), 4.77 (s, 2H, OCH<sub>2</sub>), 4.33 (t, *J* 6.8 Hz, 2H, OCH<sub>2</sub>), 3.59 (t, *J* 5.5 Hz, 2H, NCH<sub>2</sub>), 2.71 (s, 1H, OH), 2.08 – 1.96 (m, 2H, CH<sub>2</sub>), 0.93 (s, 9H, 3 x CH<sub>3</sub>), 0.08 (s, 6H, 2 x CH<sub>3</sub>); <sup>13</sup>C NMR (105 MHz, CDCl<sub>3</sub>) δ 139.3 (ArC), 137.2 (ArC), 127.6 (ArC), 121.8 (ArCH), 120.9 (ArCH), 119.5 (ArCH), 109.8 (ArCH), 101.8 (ArCH), 59.7 (OCH<sub>2</sub>), 57.0 (OCH<sub>2</sub>), 39.8 (NCH<sub>2</sub>), 32.7 (CH<sub>2</sub>), 25.9 (3 x CH<sub>3</sub>), 18.3 (C(CH<sub>3</sub>)<sub>3</sub>), -5.29 (2 x CH<sub>3</sub>); IR (ATR, cm<sup>-1</sup>) 3351, 2928, 1461, 1253, 1092; HRMS calcd for C<sub>18</sub>H<sub>29</sub>NO<sub>2</sub>Si [M<sup>+</sup>], 319.1968, found 319.1897; R<sub>f</sub> = 0.10 (10% EtOAc/Hexane).

**1-[2'-(*tert*-Butyldimethylsilyloxy)ethyl]-1*H*-indole-2-carbaldehyde (24a).** To a solution of alcohol **23a** (2.9 g, 9.9 mmol) in dry MeCN (100 mL) in a two-neck round-bottom flask was added MnO<sub>2</sub> (8.4 g, 96 mmol, 10 equiv.) and the reaction mixture was stirred at RT under N<sub>2</sub> for 8 h. The reaction mixture was filtered through Celite and the plug washed with EtOAc (80 mL). The orange colored filtrate afforded carbaldehyde **24a** as a light yellow oily solid (2.4 g, 83%), which required no further purification and was used directly in the next reaction. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 9.88 (s, 1H, CHO), 7.71 (d, *J* 8.1 Hz, 1H, ArH), 7.52 (d, *J* 8.5 Hz, 1H, ArH), 7.39 – 7.36 (m, 1H, ArH), 7.28 (s, 1H, ArH), 7.20 – 7.11 (m, 1H, ArH), 4.66 (t, *J* 5.2 Hz, 2H, OCH<sub>2</sub>), 3.95 (t, *J* 5.2

Hz, 2H, NCH<sub>2</sub>), 0.73 (s, 9H, 3 × CH<sub>3</sub>), -0.23 (s, 6H, 2 × CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 182.7 (CO), 141.5 (ArC), 135.4 (ArC), 126.9 (ArC), 126.4 (ArCH), 123.2 (ArCH), 121.0 (ArCH), 118.3 (ArCH), 111.9 (ArCH), 63.2 (OCH<sub>2</sub>), 47.1 (NCH<sub>2</sub>), 25.9 (3 × CH<sub>3</sub>), 18.2 (C(CH<sub>3</sub>)<sub>3</sub>), -5.7 (2 × CH<sub>3</sub>); IR (ATR, cm<sup>-1</sup>) 2953, 2925, 2854, 2804, 2726, 1668, 1249; HRMS calcd for C<sub>17</sub>H<sub>26</sub>NO<sub>2</sub>Si<sup>+</sup> [M+H]<sup>+</sup>, 304.1733, found 304.1730; R<sub>f</sub> = 0.79 (EtOAc/Hexane, 2:8).

**1-[3'-(*tert*-Butyldimethylsilyloxy)propyl]-1*H*-indole-2-carbaldehyde (24b).** The compound **24b** was synthesized in a similar manner to **24a** making use of the following reagents: alcohol **23b** (1.00 g, 3.13 mmol) and MnO<sub>2</sub> (5.44 g, 62.6 mmol) to produce aldehyde **24b** as a clear oil (1.00 g, 100%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 9.87 (s, 1H, CHO), 7.72 (d, *J* 8.1 Hz, 1H, ArH), 7.52 (d, *J* 8.5 Hz, 1H, ArH), 7.40 (app. t, dd, *J* 7.3 Hz, 1H, ArH), 7.26 (s, 1H, ArH), 7.16 (app. t, dd, *J* 7.5 Hz, 1H, ArH), 4.64 (t, *J* 7.1 Hz, 2H, OCH<sub>2</sub>), 3.62 (t, *J* 5.8 Hz, 2H, NCH<sub>2</sub>), 2.04 – 1.93 (m, 2H, CH<sub>2</sub>), 0.94 (s, 9H, 3 × CH<sub>3</sub>), 0.06 (s, 6H, 2 × CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 182.5 (CO), 140.6 (ArC), 135.3 (ArC), 126.8 (ArCH), 126.2 (ArC), 123.3 (ArCH), 120.9 (ArCH), 117.9 (ArCH), 111.0 (ArCH), 60.0 (OCH<sub>2</sub>), 41.7 (NCH<sub>2</sub>), 33.7 (CH<sub>2</sub>), 25.9 (3 × CH<sub>3</sub>), 18.3 (C(CH<sub>3</sub>)<sub>3</sub>), -5.4 (2 × CH<sub>3</sub>); IR (ATR, cm<sup>-1</sup>) 2856, 1665, 1460, 1319, 1249, 1110; HRMS calcd for C<sub>18</sub>H<sub>27</sub>NO<sub>2</sub>Si [M<sup>+</sup>], 317.1811, found, 317.1790; R<sub>f</sub> = 0.15 (2% EtOAc/Hexane).

**1-[2'-(*tert*-Butyldimethylsilyloxy)ethyl]-2-vinyl-1*H*-indole (25a).** To a dry, two-neck round-bottom flask charged with MePPh<sub>3</sub>Br (5.58 g, 15.6 mmol, 6 equiv.) under N<sub>2</sub> was added THF (80 mL) and the contents stirred at 0 °C for 10 min. *n*-BuLi (9.87 mL, 14.3 mmol, 5.5 equiv.) was then slowly added drop-wise to the mixture. The ice bath was removed and the reaction mixture was stirred for 30 min at 30 °C. Carbaldehyde (**24a**) (0.79 g, 2.6 mmol) in THF (15 mL) was added drop-wise to the methylenetriphenylphosphorane solution at 0 °C. The reaction mixture was stirred at RT for 8 h followed by dilution with Et<sub>2</sub>O (100 mL) and washing of the organic phase with H<sub>2</sub>O (2 × 100 mL). The combined aqueous layers were extracted with Et<sub>2</sub>O (2 × 80 mL). The organic layers were combined, washed with brine (150 mL), dried (MgSO<sub>4</sub>) and the residue was purified by chromatography (EtOAc/Hexane, 3:97) affording **25a** as an opaque oil (0.62 g, 79%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.49 (d, *J* 7.8 Hz, 1H, ArH), 7.23 (d, *J* 8.2 Hz, 1H, ArH), 7.09 (dd, *J* 8.2, 7.0 Hz, 1H, ArH), 7.03 – 6.98 (m, 1H, ArH), 6.77 (dd, *J* 17.4, 11.2 Hz, 1H, H-1'), 6.62 (s, 1H, ArH), 5.76 (dd, *J* 17.4, 1.3 Hz, 1H, *trans* H-2'), 5.26 (dd, *J* 11.2, 1.3 Hz, 1H, *cis* H-2'), 4.20 (t, *J* 6.1 Hz, 2H, OCH<sub>2</sub>), 3.81 (t, *J* 6.1 Hz, 2H, NCH<sub>2</sub>), 0.75 (s, 9H, 3 × CH<sub>3</sub>), -0.21 (s, 6H, 2 × CH<sub>3</sub>); <sup>13</sup>C NMR (105 MHz, CDCl<sub>3</sub>) δ 138.6 (ArC), 137.5 (ArC), 128.0 (ArC), 126.4 (C-1'), 121.7 (ArCH), 120.6 (ArCH), 119.9 (C-2'), 116.4 (ArCH), 109.6 (ArCH), 99.0 (ArCH), 62.3 (OCH<sub>2</sub>), 45.6 (NCH<sub>2</sub>), 26.0 (3 × CH<sub>3</sub>), 18.4 (C(CH<sub>3</sub>)<sub>3</sub>), -5.6 (2 × CH<sub>3</sub>); IR (ATR, cm<sup>-1</sup>) 3052, 2926, 2854, 1251; HRMS calcd for C<sub>18</sub>H<sub>28</sub>NOSi<sup>+</sup> [M+H]<sup>+</sup>, 302.1940, found 302.1941; R<sub>f</sub> = 0.75 (EtOAc/Hexane, 1:9).

**1-[3'-(*tert*-Butyldimethylsilyloxy)propyl]-2-vinyl-1*H*-indole (25b).** Vinyl indole **25b** was synthesised by a similar protocol as for **25a** making use of the following reagents: MePPh<sub>3</sub>Br (1.39 g, 3.89 mmol), *n*BuLi (2.35 mL, 3.29 mmol) and aldehyde **24b** (0.953 g, 3.00 mmol) to afford diene **25b** as an opaque oil (0.543 g, 55%). This compound was rather unstable during handling, and, after a sample was sent for <sup>1</sup>H NMR spectroscopy, the rest was used directly in the next reaction. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.56 (d, *J* 7.8 Hz, 1H, ArH), 7.34 (d, *J* 8.2 Hz, 1H, ArH), 7.16 (app. t, dd, *J* 7.1 Hz, 1H, ArH), 7.07 (app. t, dd, *J* 7.1 Hz, 1H, ArH), 6.85 (dd, *J* 17.4, 11.2 Hz, 1H, H-1'), 6.69 (s, 1H, ArH), 5.83 (dd, *J* 17.4, 1.2 Hz, 1H, *trans* H-2'), 5.32 (dd, *J* 11.2, 1.2 Hz, 1H, *cis* H-2'), 4.28 (t, *J* 7.0 Hz, 2H, OCH<sub>2</sub>), 3.59 (t, *J* 5.6 Hz, 2H, NCH<sub>2</sub>), 1.99 – 1.88 (m, 2H, CH<sub>2</sub>), 0.94 (s, 9H, 3 × CH<sub>3</sub>), 0.07 (s, 6H, 2 × CH<sub>3</sub>); R<sub>f</sub> = 0.59 (5% EtOAc/Hexane).

**6-[2'-(*tert*-Butyldimethylsilyloxy)ethyl]-4,5,6,10c-tetrahydropyrrolo[3,4-*c*]carbazole-1,3(2*H*,3*aH*)-dione (26a)** A neat mixture of vinyl indole **25a** (0.190 g, 0.630 mmol) and maleimide (0.073 g, 0.76 mmol, 1.2 equiv.) was heated in an oil bath at 170 °C whilst stirring for 30 min. Purification of the crude product by chromatography (EtOAc/Hexane, 3:7) afforded the dione adduct (**26a**) as a light orange solid (0.155 g) and 0.040 g of indole **25a** was recovered. Yield: 62% (78% brsm). Mp 140 – 142 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 10.95 (s, 1H, NH),

7.73 (d, *J* 7.6 Hz, 1H, ArH), 7.37 (d, *J* 7.9 Hz, 1H, ArH), 7.11 – 6.97 (m, 2H, ArH), 4.23 – 4.14 (m, 3H, CH & OCH<sub>2</sub>), 3.84 – 3.76 (m, 2H, NCH<sub>2</sub>), 3.52 – 3.39 (m, 1H, CH), 2.92 – 2.80 (m, 1H, CH<sub>2</sub>), 2.59– 2.51 (m, 1H, CH<sub>2</sub>), 2.37 – 2.22 (m, 1H, CH<sub>2</sub>), 1.85 – 1.69 (m, 1H, CH<sub>2</sub>), 0.70 (s, 9H, 3 × CH<sub>3</sub>), -0.27 (s, 6H, 2 × CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 180.3 (CO), 178.6 (CO), 136.5 (ArC), 136.1 (ArC), 126.3 (ArC), 120.7 (ArCH), 119.5 (ArCH), 118.8 (ArCH), 109.5 (ArCH), 102.8 (ArC), 61.8 (OCH<sub>2</sub>), 44.7 (NCH<sub>2</sub>), 40.7 (CH), 40.5 (CH), 25.7 (3 × CH<sub>3</sub>), 20.9 (C(CH<sub>3</sub>)<sub>3</sub>), 18.4 (CH<sub>2</sub>) 17.9 (CH<sub>2</sub>), -5.8 (2 × CH<sub>3</sub>); HRMS calcd for C<sub>22</sub>H<sub>31</sub>N<sub>2</sub>O<sub>3</sub>Si<sup>+</sup> [M+H]<sup>+</sup>, 399.2104, found 399.2109; IR (ATR, cm<sup>-1</sup>) 3181, 2951, 2928, 2854, 1700, 1250; R<sub>f</sub> = 0.21 (20% EtOAc/Hexane).

**6-[2<sup>1</sup>-(*tert*-Butyldimethylsilyloxy)propyl]-4,5,6,10c-tetrahydropyrrolo[3,4-*c*]carbazole-1,3(2*H*,3*aH*)-dione (26b)**

Dione **26b** was prepared by a similar pyrolysis protocol as for **26a** using the following: diene **25b** (0.534 g, 1.69 mmol) and maleimide (0.213 g, 2.19 mmol) affording a green, viscous oil which later solidified (0.633 g, 91%). mp = 131 – 132 °C (from dioxane/hexane); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 7.99 (s, 1H, NH), 7.93 – 7.90 (m, 1H, ArH), 7.33 – 7.31 (m, 1H, ArH), 7.21 – 7.12 (m, 2H, ArH), 4.33 (d, *J* 8.0, 1H, CH), 4.18 – 4.08 (m, 2H, CH<sub>2</sub>), 3.61 – 3.49 (m, 2H, CH<sub>2</sub>), 3.45 – 3.41 (m, 1H, CH), 2.88 – 2.83 (m, 1H, CH<sub>2</sub>), 2.71 – 2.66 (m, 1H, CH<sub>2</sub>), 2.61 – 2.54 (m, 1H, CH<sub>2</sub>), 1.97 – 1.84 (m, 3H, CH and CH<sub>2</sub>), 0.93 (s, 9H, 3 × CH<sub>3</sub>), 0.06 (s, 6H, 2 × CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 179.0 (CO), 177.1 (CO), 136.4 (ArC), 135.8 (ArC), 126.4 (ArC), 121.6 (ArCH), 119.8 (ArCH), 119.7 (ArCH), 109.2 (ArCH), 102.2 (ArC), 59.5 (OCH<sub>2</sub>), 41.5 (NCH<sub>2</sub>), 41.1 (CH), 39.5 (CH), 33.1 (CH<sub>2</sub>), 25.9 (3 × CH<sub>3</sub>), 21.3 (CH<sub>2</sub>), 18.4 (CH<sub>2</sub>), 18.2 (C(CH<sub>3</sub>)<sub>3</sub>), -5.4 (2 × CH<sub>3</sub>); IR (ATR, cm<sup>-1</sup>) 3235, 2937, 1701, 1463, 1340, 1164; HRMS: calcd for C<sub>23</sub>H<sub>32</sub>N<sub>2</sub>O<sub>3</sub>Si [M<sup>+</sup>], 412.2182, found 412.2180; R<sub>f</sub> = 0.37 (50% EtOAc/Hexane).

**6-(2<sup>1</sup>-Hydroxyethyl)-4,5,6,10c-tetrahydropyrrolo[3,4-*c*]carbazole-1,3(2*H*,3*aH*)-dione (27)**. To a dry two-neck round-bottom flask containing dione **26a** (0.256 g, 0.642 mmol) in THF (8 mL) in an ice bath was added in one portion TBAF·3H<sub>2</sub>O (1.01 g 3.21 mmol, 5 equiv.), followed by stirring at RT under N<sub>2</sub> for 30 min. CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was added to the reaction mixture and the organic phase was washed with saturated aqueous NaHCO<sub>3</sub> (20 mL). The aqueous layer was collected and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 20 mL). The organic layers were combined and washed with brine (50 mL), dried (MgSO<sub>4</sub>) and the residue obtained purified by chromatography (EtOAc/Hexane, 7:3) to afford alcohol **27** as a yellow solid (0.155 g, 86%). Mp 166 – 169 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 10.97 (s, 1H, NH), 7.74 (d, *J* 7.5 Hz, 1H, ArH), 7.39 (d, *J* 7.9 Hz, 1H, ArH), 7.12 – 6.97 (m, 2H, ArH), 4.84 (s, 1H, OH), 4.24 – 4.10 (m, 3H, CH & OCH<sub>2</sub>), 3.66 – 3.57 (m, 2H, NCH<sub>2</sub>), 3.51 – 3.42 (m, 1H, CH), 2.93 – 2.80 (m, 1H, CH<sub>2</sub>), 2.60 – 2.52 (m, 1H, CH<sub>2</sub>), 2.35 – 2.24 (m, 1H, CH<sub>2</sub>), 1.90 – 1.73 (m, 1H, CH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 180.4 (CO), 178.7 (CO), 136.6 (ArC), 136.2 (ArC), 126.3 (ArC), 120.7 (ArCH), 119.5 (ArCH), 118.8 (ArCH), 109.4 (ArCH), 102.6 (ArC), 60.1 (OCH<sub>2</sub>), 45.1 (NCH<sub>2</sub>), 40.7 (CH), 40.5 (CH), 21.1 (CH<sub>2</sub>), 18.4 (CH<sub>2</sub>); HRMS calcd for C<sub>16</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub><sup>+</sup> [M+H]<sup>+</sup>, 285.1239, found 285.1246; IR (ATR, cm<sup>-1</sup>) 3421, 1704; R<sub>f</sub> = 0.39 (EtOAc/Hexane, 8:2).

**6-(2<sup>1</sup>-Hydroxyethyl)pyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione (29a)**. To a two-neck round-bottom flask charged with dione **27** (0.188 g, 0.661 mmol) in dry dioxane (15 mL) under argon, was added MnO<sub>2</sub> (1.26 g, 14.5 mmol, 22 equiv.), and the reaction mixture was stirred and heated at reflux for 18 h. The spent MnO<sub>2</sub> was removed by filtration through Celite and the residue was purified by chromatography (EtOAc/Hexane, 8:2) to afford aryl dione **29a** as a yellow solid (0.098 g, 53%). Mp 322 – 324 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 11.15 (s, 1H, NH), 8.87 (d, *J* 7.8 Hz, 1H, ArH), 8.01 (d, *J* 8.3 Hz, 1H, ArH), 7.84 (d, *J* 8.3 Hz, 1H, ArH), 7.75 (d, *J* 8.2 Hz, 1H, ArH), 7.62 (app. t, dd, *J* 7.6 Hz, 1H, ArH), 7.36 (app. t, dd, *J* 7.4 Hz, 1H, ArH), 4.90 (t, *J* 4.9 Hz, 1H, OH), 4.55 (d, *J* 4.4 Hz, 2H, OCH<sub>2</sub>), 3.82 (d, *J* 4.8 Hz, 2H, NCH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 171.0 (CO), 170.9 (CO), 145.3 (ArC), 142.9 (ArC), 128.7 (ArC), 127.3 (ArCH), 125.4 (ArC), 124.5 (ArC), 120.9 (ArCH), 120.4 (ArCH), 119.9 (ArCH), 118.7 (ArC), 115.2 (ArCH), 111.1 (ArCH), 60.2 (OCH<sub>2</sub>), 46.4 (NCH<sub>2</sub>); HRMS calcd for C<sub>16</sub>H<sub>13</sub>N<sub>2</sub>O<sub>3</sub><sup>+</sup> [M+H]<sup>+</sup>, 281.0926, found 281.0937; IR (ATR, cm<sup>-1</sup>) 3372, 1710; R<sub>f</sub> = 0.57 (EtOAc/Hexane, 8:2).

**6-[3'-(tert-Butyldimethylsilyloxy)propyl]pyrrolo[3,4-c]carbazole-1,3(2H,6H)-dione (28).** To a round-bottom flask containing a solution of indole **26b** (0.738 g, 0.179 mmol) in dry dioxane (15 mL) was added MnO<sub>2</sub> (1.55 g, 17.8 mmol) and the reaction mixture heated at reflux under argon for 4 h. The cooled reaction mixture was filtered through celite to give an orange solution. The solid residue obtained was recrystallized twice from dioxane/hexane (66% dioxane: 33% hexane), affording bright orange crystals of aryl dione **28** (0.542 g, 63%). mp = 205 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 9.02 (d, *J* 7.9 Hz, 1H, ArH), 7.90 (d, *J* 8.3 Hz, 1H, ArH), 7.77 (d, *J* 8.4 Hz, 1H, ArH), 7.67 (s, 1H, NH), 7.65 – 7.50 (m, 2H, ArH), 7.39 (app. t, dd, *J* 7.4 Hz, ArH), 4.53 (t, *J* 6.7 Hz, 2H, OCH<sub>2</sub>), 3.59 (t, *J* 5.4 Hz, 2H, NCH<sub>2</sub>), 2.15 – 1.99 (m, 2H, CH<sub>2</sub>), 0.97 (s, 9H, 3 × CH<sub>3</sub>), 0.08 (s, 6H, 2 × CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 169.4 (CO), 169.0 (CO), 144.9 (ArC), 142.2 (ArC), 128.4 (ArC), 126.9 (ArCH), 126.1 (ArC), 123.9 (ArC), 121.0 (ArCH), 120.6 (ArCH), 119.9 (ArCH), 119.6 (ArC), 113.3 (ArCH), 109.2 (ArCH), 59.3 (OCH<sub>2</sub>), 39.9 (NCH<sub>2</sub>), 31.8 (CH<sub>2</sub>), 25.9 (3 × CH<sub>3</sub>), 18.3 (C(CH<sub>3</sub>)<sub>3</sub>), -5.3 (2 × CH<sub>3</sub>); HRMS calc for C<sub>23</sub>H<sub>29</sub>N<sub>2</sub>O<sub>3</sub>Si 408.1869, found 408.1867; IR (ATR, cm<sup>-1</sup>) 3233, 2951, 1709, 1290, 1084, 1042; R<sub>f</sub> = 0.30 (40% EtOAc/Hexane).

**6-(3'-Hydroxypropyl)pyrrolo[3,4-c]carbazole-1,3(2H,6H)-dione (29b).** To a round-bottom flask containing a solution of silyl-carbazole **28** (0.133 g, 0.325 mmol), in dry THF (5 mL) was added tetrabutylammonium fluoride (TBAF).3H<sub>2</sub>O in one portion (0.52 mL, 0.52 mmol) under argon and the reaction mixture was stirred for 30 min at RT. Saturated aqueous NH<sub>4</sub>Cl was added and the reaction mixture was diluted with EtOAc (100 mL). The phases were separated and the aqueous layer was extracted using EtOAc (3 × 100 mL). The organic phases were combined, washed with brine (100 mL), dried (MgSO<sub>4</sub>) and filtered. The solid product obtained by evaporation of the solvent was recrystallized from THF and hexane (70% THF: 30% hexane) to afford aryl dione **29b** as bright orange crystals (0.0625 g, 65%). Mp 210 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 11.16 (s, 1H, NH), 8.86 (d, *J* 7.8 Hz, 1H, ArH), 8.00 (d, *J* 8.4 Hz, 1H, ArH), 7.85 (d, *J* 8.3 Hz, 1H, ArH), 7.75 (d, *J* 8.3 Hz, 1H, ArH), 7.63 (app. t, dd, *J* 7.7 Hz, 1H, ArH), 7.36 (app. t, dd, *J* 7.4 Hz, 1H, ArH), 4.72 – 4.69 (m, 1H, OH), 4.56 (t, *J* 6.8 Hz, 2H, OCH<sub>2</sub>), 3.46 – 3.36 (m, 2H, NCH<sub>2</sub>), 2.19 – 1.89 (m, 2H, CH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>, note: NCH<sub>2</sub> masked by DMSO-*d*<sub>6</sub> septet) δ 170.3 (CO), 170.2 (CO), 144.1 (ArC), 141.8 (ArC), 128.2 (ArC), 126.8 (ArCH), 124.9 (ArC), 123.9 (ArC), 120.3 (ArCH), 119.7 (ArCH), 119.5 (ArCH), 118.0 (ArC), 113.9 (ArCH), 110.01 (ArCH), 57.7 (OCH<sub>2</sub>), 31.5 (CH<sub>2</sub>); IR (ATR, cm<sup>-1</sup>) 3437, 3155, 2943, 1710, 1448, 1313; HRMS calcd for C<sub>17</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>, 294.1004, found 294.0989.

**1-(2'-Propynyl)-2-vinyl-1H-indole (30a).** To a two-neck round-bottom flask containing substituted indole **13** (0.505 g, 3.53 mmol) in dry DMF (80 mL) under argon was added Cs<sub>2</sub>CO<sub>3</sub> (3.45 g, 10.6 mmol, 3 equiv.) and propargyl bromide (1.51 g, 10.6 mmol, 3 equiv.). The reaction mixture was stirred at 60 °C for 2 d under argon, cooled to RT and then diluted with EtOAc (50 mL) and washed with H<sub>2</sub>O (3 × 50 mL). The organic layers were combined, washed with brine (150 mL) and dried over MgSO<sub>4</sub>. The residue was purified by chromatography (EtOAc/Hexane, 5:95) to obtain indole product **30a** as a yellow solid (0.29 g, 45%). The <sup>1</sup>H NMR spectrum of **30a** compared well to that in the literature.<sup>37</sup> <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.59 (d, *J* 7.8 Hz, 1H, ArH), 7.38 (d, *J* 8.2 Hz, 1H, ArH), 7.28 – 7.24 (m, 1H, ArH), 7.15 – 7.11 (m, 1H, ArH), 6.90 (dd, *J* 17.4, 11.2, Hz, 1H, H-1'), 6.73 (s, 1H, ArH), 5.86 (dd, *J* 17.4, 0.7 Hz, 1H, *trans* H-2'), 5.43 (dd, *J* 11.2, 0.7 Hz, 1H, *cis* H-2'), 4.90 (d, *J* 2.4 Hz, 2H, NCH<sub>2</sub>), 2.31 (t, *J* 2.4 Hz, 1H, CH); R<sub>f</sub> = 0.68 (EtOAc/Hexane, 1:9).

**6-(2'-Propynyl)-4,5,6,10c-tetrahydropyrrolo[3,4-c]carbazole-1,3(2H,3aH)-dione (31a).** A neat mixture of indole **30a** (0.114 g, 0.629 mmol) and maleimide (0.092 g 0.94 mmol, 1.5 equiv.) in a round-bottom flask (5 mL) was placed in an oil bath pre-heated to 160 °C. The mixture solidified within a few seconds. The reaction mixture was kept at this temperature for 30 min and the brown solid was washed with CH<sub>2</sub>Cl<sub>2</sub> (40 mL) and this fraction was purified by chromatography (EtOAc/Hexane, 3:7) affording 0.048 g of adduct **31a** as a light yellow solid, together with unreacted **30a** (0.040 gm). The CH<sub>2</sub>Cl<sub>2</sub> insoluble dark brown solid was pure adduct **31a** (0.035g) for a total of 0.083 g (47% and 73% brsm). Mp 252 – 254 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 11.03 (s,

1H, NH), 7.77 (d, *J* 7.6 Hz, 1H, ArH), 7.49 (d, *J* 7.9 Hz, 1H, ArH), 7.20 – 7.02 (m, 2H, ArH), 5.00 (s, 2H, NCH<sub>2</sub>), 4.21 (d, *J* 7.7 Hz, 1H, CH), 3.54 – 3.42 (m, 1H, CH), 3.28 (s, 1H, CH), 2.93 – 2.81 (m, 1H, CH<sub>2</sub>), 2.64 – 2.54 (m, 1H, CH<sub>2</sub>), 2.39 – 2.24 (m, 1H, CH<sub>2</sub>), 1.85 (dd, *J* 14.1, 9.1 Hz, 1H, CH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 180.7 (CO), 179.0 (CO), 136.3 (ArC), 136.1 (ArC), 126.8 (ArC), 121.7 (ArCH), 120.2 (ArCH), 119.8 (ArCH), 109.9 (ArCH), 104.4 (ArC), 79.9 (CCH), 75.2 (CCH), 41.1 (NCH<sub>2</sub>), 40.9 (CH), 32.2 (CH), 21.4 (CH<sub>2</sub>), 18.5 (CH<sub>2</sub>); HRMS calcd for C<sub>17</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>, 279.1134, found 279.1126; IR (ATR, cm<sup>-1</sup>) 3293, 1700; R<sub>f</sub> = 0.45 (EtOAc/Hexane, 4:8).

**6-(2'-Propynyl)pyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione (32a).** To a two-neck round-bottom flask containing a solution of dione **31a** (0.120 g, 0.43 mmol) in dry dioxane (15 mL) was added MnO<sub>2</sub> (0.825 g, 9.49 mmol, 22 equiv.), and the reaction mixture was stirred and heated under reflux for 8 h. The cooled reaction mixture was filtered through celite and the plug washed with dioxane (20 mL). The crude product obtained by removal of the solvent was triturated with CH<sub>2</sub>Cl<sub>2</sub> and acetone to afford the aryl dione **32a** as a yellow solid (0.092 g, 72%). mp = 278 – 280 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 11.22 (s, 1H, NH), 8.87 (d, *J* 7.9 Hz, 1H, ArH), 8.08 (d, *J* 8.3 Hz, 1H, ArH), 7.90 (d, *J* 8.3 Hz, 1H, ArH), 7.83 (d, *J* 8.2 Hz, 1H, ArH), 7.67 (app. t, dd, *J* 7.6 Hz, 1H, ArH), 7.40 (app. t, dd, *J* 7.6 Hz, 1H, ArH), 5.46 (s, 2H, NCH<sub>2</sub>), 3.56 (s, 1H, CCH); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 170.1 (CO), 170.1 (CO), 143.6 (ArC), 141.3 (ArC), 128.4 (ArC), 126.9 (ArCH), 125.0 (ArC), 124.7 (ArC), 121.0 (ArCH), 120.1 (ArCH), 119.8 (ArCH), 118.5 (ArC), 114.3 (ArCH), 110.3 (ArCH), 78.4 (CCH), 75.1 (CCH), 32.4 (CH<sub>2</sub>); HRMS calcd for C<sub>17</sub>H<sub>11</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>, 275.0821, found 275.0316; IR (ATR, cm<sup>-1</sup>) 3271, 1720, 1701; R<sub>f</sub> = 0.84 (EtOAc/Hexane, 7:3).

**3-(2'-Vinyl-1*H*-indol-1'-yl)propanenitrile (30b).** To a two-neck round-bottom flask containing a solution of disubstituted indole **13** (0.750 g, 5.24 mmol) in dry MeCN (20 mL) under argon, was added acrylonitrile (2.40 mL, 36.7 mmol, 7 equiv.), followed by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 20 drops). The reaction mixture was stirred at RT under argon for 8 h and then diluted with H<sub>2</sub>O (30 mL) and extracted with EtOAc (30 mL). The organic layer was washed with brine (50 mL) and dried over MgSO<sub>4</sub>. The crude product was purified by chromatography (EtOAc/Hexane, 1:9) to afford the propanenitrile **30b** as an opaque solid (0.750 g), together with unreacted indole **13** (0.098 g) Yield: 73% (84% brsm). Mp 83 – 85 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.59 (d, *J* 7.8 Hz, 1H, ArH), 7.29 – 7.20 (m, 2H, ArH), 7.16 – 7.11 (m, 1H, ArH), 6.76 (dd, *J* 17.3, 11.2, 1H, H-1'), 6.72 (s, 1H, ArH), 5.86 (d, *J* 17.3 Hz, 1H, *trans* H-2'), 5.44 (d, *J* 11.2 Hz, 1H, *cis* H-2'), 4.47 (t, *J* 7.2 Hz, 2H, NCH<sub>2</sub>), 2.73 (t, *J* 7.2 Hz, 2H, CCH<sub>2</sub>); <sup>13</sup>C NMR (105 MHz, CDCl<sub>3</sub>) δ 137.6 (ArC), 136.7 (ArC), 128.4 (ArC), 125.0 (C-1'), 122.6 (ArCH), 121.2 (ArCH), 120.8 (ArCH), 118.1 (CN), 117.1 (C-2'), 108.8 (ArCH), 100.8 (ArCH), 39.0 (NCH<sub>2</sub>), 18.6 (CH<sub>2</sub>); HRMS calcd for C<sub>13</sub>H<sub>13</sub>N<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>, 197.1079, found 197.1072; IR (ATR, cm<sup>-1</sup>) 2247; R<sub>f</sub> = 0.22 (EtOAc/Hexane, 1:9).

**3-{1',3'-Dioxo-1',2',3',3*a*',4',5'-hexahydropyrrolo[3,4-*c*]carbazol-6(10*cH*)-yl}-propanenitrile (31b).** To a solution of propanenitrile **30b** (0.280 g, 1.43 mmol) in toluene (15 mL) under N<sub>2</sub> was added maleimide (0.208 g, 2.14 mmol, 1.5 equiv.) and SnCl<sub>2</sub> (0.005 g, 0.03 mmol, 0.02 equiv.), and the reaction mixture was heated with stirring under reflux for 16 h. Saturated NaHCO<sub>3</sub> (30 mL) was added to the cold mixture and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 30 mL). The combined organic layers were then washed with brine (80 mL) and dried over MgSO<sub>4</sub>. The residue was purified by chromatography (EtOAc/Hexane, 1:1). This led to the recovery of propanenitrile **30b** (0.050 g), followed by the product **31b** as a yellow solid (0.243 g). Yield: 58% (71% brsm). Mp 160 – 162 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 11.02 (s, 1H, NH), 7.76 (d, *J* 7.5 Hz, 1H, ArH), 7.51 (d, *J* 8.0 Hz, 1H, ArH), 7.17 – 7.02 (m, 2H, ArH), 4.43 (t, *J* 6.3 Hz, 2H, NCH<sub>2</sub>), 4.21 (d, *J* 8.0 Hz, 1H, CH), 3.54 – 3.43 (m, 1H, CH), 2.92 (t, *J* 6.3 Hz, 2H, CCH<sub>2</sub>), 2.88 – 2.82 (m, 1H, CH<sub>2</sub>), 2.67 – 2.55 (m, 1H, CH<sub>2</sub>), 2.38 – 2.25 (m, 1H, CH<sub>2</sub>), 1.90 – 1.75 (m, 1H, CH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 180.3 (CO), 178.5 (CO), 135.9 (ArC), 135.7 (ArC), 126.5 (ArC), 121.1 (ArCH), 119.7 (ArCH), 119.4 (CN), 118.9 (ArCH), 109.5 (ArCH), 103.7 (ArC), 40.6 (CH), 38.7 (CH<sub>2</sub>),

38.0 (CH), 21.1 (CH<sub>2</sub>), 18.2 (CH<sub>2</sub>), 18.0 (CH<sub>2</sub>); HRMS calcd for C<sub>17</sub>H<sub>16</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>, 294.1243, found 294.1253; IR (ATR, cm<sup>-1</sup>) 2246, 1703; R<sub>f</sub> = 0.21 (EtOAc/Hexane, 6:4).

**3-{1',3'-Dioxo-2,3-dihydropyrrolo[3,4-c]carbazol-6(1H)-yl}propanenitrile (32b).** To a two-neck round-bottom flask containing a solution of propanenitrile **31b** (0.490 g, 1.67 mmol) in dry dioxane (20 mL), and under argon, was added MnO<sub>2</sub> (3.20 g, 36.8 mmol, 22 equiv.). The reaction mixture was stirred and heated under reflux for 8 h. The cooled mixture was filtered through celite and the residue purified by recrystallization from DMF to afford the aromatized product **32b** as a yellow solid (0.145 g, 30%). Mp 298 – 300 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 11.21 (s, 1H, NH), 8.88 (d, *J* 7.8 Hz, 1H, ArH), 8.16 (d, *J* 8.3 Hz, 1H, ArH), 7.88 (d, *J* 8.5 Hz, 2H, ArH), 7.69 – 7.60 (m, 1H, ArH), 7.44 – 7.35 (m, 1H, ArH), 4.89 (t, *J* 6.3 Hz, 2H, NCH<sub>2</sub>), 3.10 (t, *J* 6.3 Hz, 2H, CCH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 170.1 (CO), 170.1 (CO), 143.8 (ArC), 141.4 (ArC), 128.3 (ArC), 126.8 (ArCH), 124.9 (ArC), 124.5 (ArC), 120.9 (ArCH), 120.0 (ArCH), 119.6 (ArCH), 118.7 (CN), 118.3 (ArC), 114.4 (ArCH), 110.3 (ArCH), 38.6 (NCH<sub>2</sub>), 17.0 (CCH<sub>2</sub>); HRMS calcd for C<sub>17</sub>H<sub>12</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>, 290.0930, found 290.0928; IR (ATR, cm<sup>-1</sup>): 2251, 1716, 1697; R<sub>f</sub> = 0.32 (EtOAc/Hexane, 6:4).

## Acknowledgements

AEvdW would like to acknowledge the South African National Research Foundation (NRF, Pretoria, South Africa) and Stellenbosch University (SU) for financial support during her PhD studies. WvO, SCP and IRG thank the NRF (CPRR and Incentive funding – Grant UIDs 93528, 109465 and 113322), and Stellenbosch University (Faculty and Departmental support) for research support. SCP also thanks School of Chemistry and Faculty of Science, University of the Witwatersrand for support. Central Analytical Facilities (CAF), Stellenbosch, and Mass and NMR Spectroscopy services at University of Witwatersrand, are also acknowledged for support in characterizing compounds.

## Supplementary Material

The <sup>1</sup>H, <sup>13</sup>C NMR spectra of Diels-Alder products (**26b**, **27**, **31a**, and **31b**) and novel substituted pyrrolocarbazoles (**28**, **29a**, **29b**, **32a** and **32b**) are available in the online supplementary information file.

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