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Metathesis Reactions for the Synthesis of Ring-Fused Carbazoles

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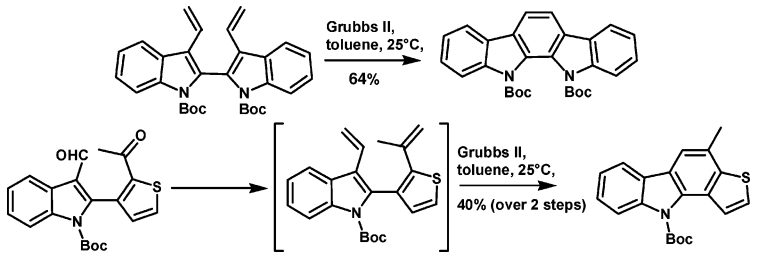

The metathesis reaction is used as a key step for the synthesis of the indolo[2,3-*a*]carbazole core of rebeccamycin **13** and the sulfur analog of furostifoline **21**. Using the same methodology for the attempted synthesis of furostifoline, we unexpectedly formed *tert*-butyl-2a-methyl-1,2,2a,10c-tetrahydro-6*H*-cyclobuta[*c*]furo[3,2-*a*]carbazole-6-carboxylate **26** from the unstable diene, *tert*-butyl 2-(2-isopropenyl-3-furyl)-3-vinyl-1*H*-indole-1-carboxylate **25**, presumably via a spontaneous π_8 electrocyclization reaction.

Introduction

The development of methods for the synthesis of fused carbazole nuclei is becoming increasingly important as a result of the number of natural and nonnatural carbazoles that display biological activity. For example, the natural carbazoles, rebeccamycin (**1a**) and furostifoline (**1b**), are important natural products that fit into this class (Figure 1).[1] Rebeccamycin binds to DNA and has anti-tumor properties,[2−6] and in fact, a rebeccamycin analog is presently undergoing clinical trials for the treatment of patients with advanced liver and/or biliary cancer and leukemia.[7−9]

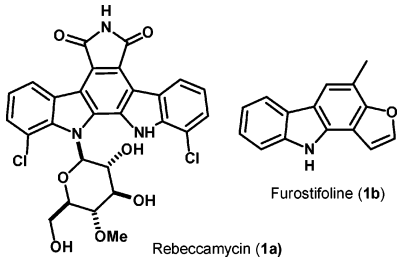

FIGURE 1. Naturally occurring [*a*]-fused carbazoles.

Furostifoline, on the other hand, was isolated in 1990 from the root bark of *Murraya euchrestifolia* Hayata and is used in Chinese folk medicine.[10] Even though the natural product is relatively simple, interest in this product has resulted in at least six syntheses of this [*a*]-fused carbazole.[10] The synthesis of furostifoline has been achieved using a variety of ways ranging from an

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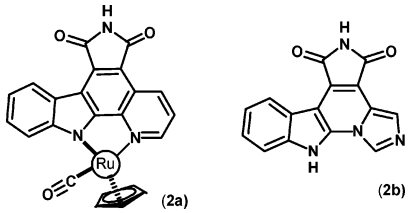


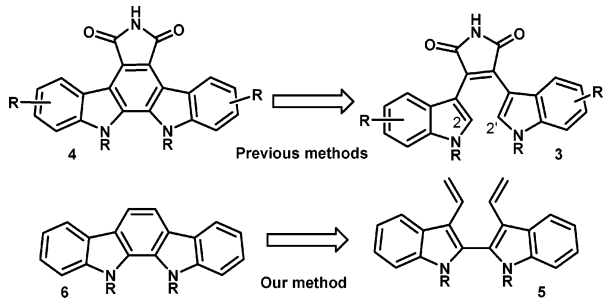
FIGURE 2. Nonnatural [*a*]-fused carbazoles.

iron-mediated method[11] to the use of thermal, reductive, and photocyclization methodologies.[12−15]

As a result of the interest in these natural products, the syntheses of many analogs that also have biological activity have been described. Two unnatural products that fit into this category are shown in Figure 2. Compound **2a** is a known organometallic inhibitor of glycogen synthase kinase 3,[16] while isogranulatimide (**2b**) is a G2 checkpoint inhibitor.[17]

Results and Discussion

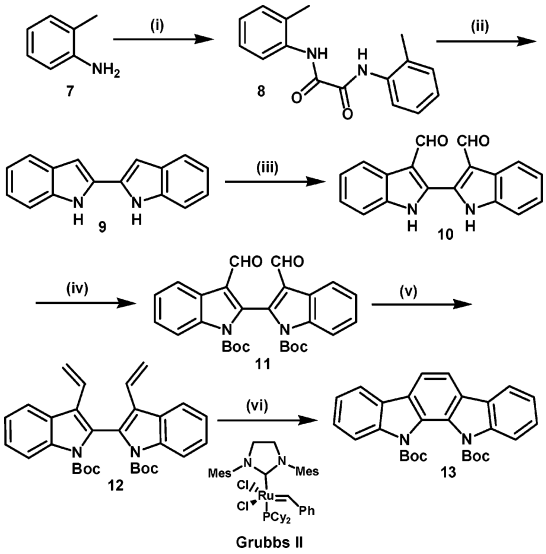
Examination of these four examples shown in Figures 1 and 2 shows that they are all fused carbazoles containing at least one additional ring fused to the [*a*]-face of the carbazole nucleus. As part of our ongoing program on the synthesis of carbazoles,[18] we wish to report in this article on the synthesis of the core of rebeccamycin, the unnatural sulfur analog of furostifoline, and our attempts at using the same methodology to make the natural product furostifoline.



Retrosynthesis

In general, the synthesis of rebeccamycin (or analogs) relies on the construction of the bond between the two indole units at C-2 and C-2′ (see retrosynthesis) as one of the last steps of the synthesis, viz. **3** → **4**.[1] In this article and in contrast to many syntheses, the construction of the bond between the two indole units at C-2 and C-2′ of the rebeccamycin nucleus takes place at an early stage of the synthesis. In addition, one of the key steps is that an aromatic ring is formed using the metathesis reaction[19] (see, for example, transformation **5** → **6**). This is one of the first examples of the use of metathesis to form an aromatic ring in one step.[20]

SCHEME 1[a]



[a] Reagents and conditions: (i) ClCOCOCl, 99%; (ii) KOBu^t, 300 °C, 80%; (iii) $POCl_3$, DMF, 0 °C, 83%; (iv) Boc_2O, DMAP, 25 °C, 89%; (v) $MePPh_2Br$, *n*-BuLi, 0 °C; (vi) 8% Grubbs II, toluene, 25 °C, 64% (over two steps).

o-Toluidine (**7**) was treated as described in the literature[21] with oxalyl chloride to give the diamide **8** in good yield. Compound **8** was then subjected to potassium *tert*-butoxide at 300 °C giving the desired bis-indole **9** in excellent yield (Scheme 1).[21] Normal Vilsmeier−Haack reaction conditions on **9** provided the required dialdehyde **10**,[21] which was readily protected as the bis-carbamate **11**.

To utilize the metathesis reaction to form the benzene ring fused to both indole nuclei, the aldehydes first had

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(20) (a) For the synthesis of phenanthrenes using ring-closing metathesis to form an aromatic ring, see: (i) Iuliano, A.; Piccioli, P.; Fabbri, D. *Org. Lett.* **2004**, *6*, 3711 and (ii) Walker, E. R.; Leung, S. Y.; Barrett, A. G. M. *Tetrahedron Lett.* **2005**, *46*, 6537. (b) Phenols, naphthols, and naphthalenes, respectively, have been made using ring-closing metathesis: (i) Yoshida, K.; Imamoto, T. *J. Am. Chem. Soc.* **2005**, *127*, 10470. (ii) van Otterlo, W. A. L.; Ngidi, E. M.; Coyanis, E. M.; de Koning, C. B. *Tetrahedron Lett.* **2003**, *44*, 311. (iii) Huang, K.-S.; Wang, E.-C. *Tetrahedron Lett.* **2001**, *42*, 6155. (c) For an example of ring-closing metathesis followed by oxidative aromatization to form a benzene ring, see: Kotha, S.; Mandal, K. *Tetrahedron Lett.* **2004**, *45*, 2585. (d) Some researchers have used the same initial retrosynthetic approach as us by using the Suzuki−Miyaura coupling reaction at an early stage to make the bis-indole 2 and 2′ linkage. See: Cai, C.; Snieckus, V. *Org. Lett.* **2004**, *6*, 2293.

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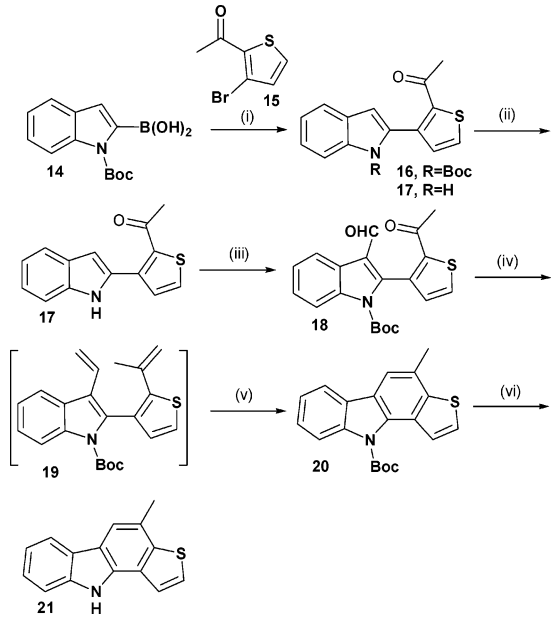
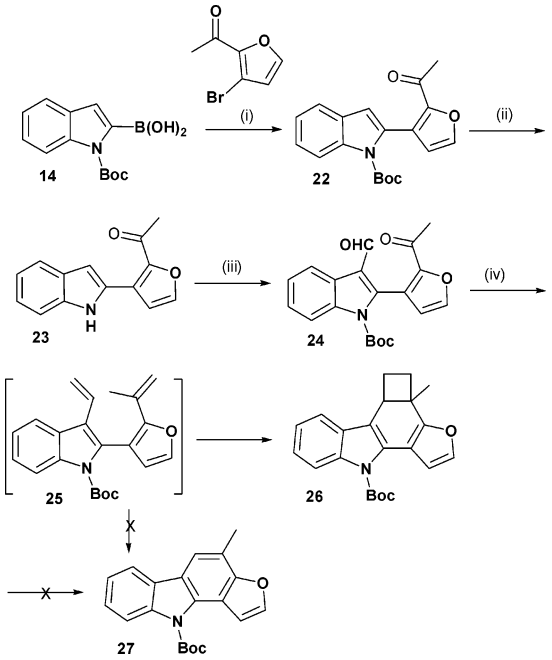
SCHEME 2[a]



[a] Reagents and conditions: (i) 10% $Pd(PPh_3)_4$, DME, aqueous Na_2CO_3, 100 °C, 78%; (ii) $AlCl_3$, CH_2Cl_2, 0 °C, 87% or SiO_2, microwave, 99%; (iii) (a) $POCl_3$, DMF, 0 °C; (b) Boc_2O, DMAP, 25 °C, 50% (over two steps); (iv) $MePPh_2Br$, *n*-BuLi, 0 °C; (v) 11% Grubbs II, toluene, 25 °C, 40% (over two steps); (vi) TFA, CH_2Cl_2, reflux, 72%.

SCHEME 3[a]



[a] Reagents and conditions: (i) 10% $Pd(PPh_3)_4$, DME, aqueous Na_2CO_3, 100 °C, 78%; (ii) (a) $AlCl_3$, CH_2Cl_2, 0 °C, 84%; or (b) silica gel, microwave, 83%; (iii) (a) $POCl_3$, DMF, 0 °C; (b) Boc_2O, DMAP, 25 °C, 79%; (iv) $MePPh_2Br$, *n*-BuLi, 0 °C, 28% (**24** → **26**).

to be converted into alkenes. This was readily achieved using the Wittig reaction to give **12**. Exposure of **12** to the Grubbs second-generation catalyst then gave the desired indole-fused carbazole **13** in 64% yield.

Since the previous synthesis was successful, the synthesis of a product containing a thiophene fused to the carbazole nucleus rather than an indole was attempted. This would constitute the synthesis of a sulfur analog of furostifoline (**1b**). To this end, the synthesis of the desired indole boronic acid **14** was accomplished using known methodology (Scheme 2).[18] In addition, the halogenated thiophene **15** required for the Suzuki coupling was prepared by Friedel–Crafts acylation of 3-bromothiophene to afford exclusively 2-acetyl-3-bromothiophene (**15**) using methodology similar to that used by Tanaka and coworkers.[22]

Treatment of indole boronic acid **14** with 2-acetyl-3-bromothiophene (**15**)[22b] under palladium-catalyzed conditions resulted in the formation of the required carbon–carbon bond, to yield **16** together with a 2–5% of **17** depending on the amount of solvent used. Since a small amount of **15** remained unreacted and because **17** and **15** had very similar R_f values, the crude material was treated with an excess of Boc anhydride, thus converting all **17** to **16** and enabling proper separation from unreacted **15**. Then subsequent removal of the Boc-protecting group of **16** with $AlCl_3$ gave the unprotected indole **17**.

Treatment of **17** with DMF and $POCl_3$ under Vilsmeier–Haack reaction conditions resulted in the introduction of a formyl group at the 3-position of the indole nucleus. Reaction of this intermediate with Boc_2O gave **18**, which was then subjected to Wittig conditions to afford **19**. It was noted that diene **19** was substantially more unstable than diene **12**, and it could not be concentrated down without significant decomposition taking place. To circumvent this problem, an excess of toluene was utilized to drive off the lower boiling solvents from **19**, and then without delay Grubbs catalyst was added, and the reaction was left to stir at room temperature for 21 h. After purification, the desired carbazole **20** was obtained in 40% yield over the two steps. The Boc-protecting group was then easily removed by exposure of **20** to TFA to furnish the sulfur analog of furostifoline **21** in 72% yield.

At the same time, the attempted synthesis of furostifoline (**1b**) was carried out as shown in Scheme 3. Conversion of **14** to **24** in three steps proved to be uneventful and provided the same types of intermediates as those described for the sulfur series. However, treatment of **24** using traditional Wittig reaction conditions did not afford diene **25** but gave cyclobutane **26** as the only product. It is believed that diene **25** undergoes a spontaneous π_8 electrocyclization followed by a π_6 electrocyclization reaction to afford **26**. All attempts to trap the intermediate diene **25** in situ and to react this with the Grubbs second-generation catalyst failed to yield the desired carbazole **27**. Attempts to coerce the cyclobutane **26** to undergo aromatization with the loss of ethylene to afford **27** under a range of reaction conditions were also unsuccessful.

In conclusion, we have demonstrated for the first time that the metathesis reaction can be used for the construction of the central aromatic ring of both the indolo[2,3-*a*]carbazole and the thieno[3,2-*a*]carbazole nucleus. Unfortunately, using the same methodology for the

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synthesis of the natural product furostifoline was frustratingly unsuccessful.

Experimental Section

***N,N′*-Di-*tert*-butyldicarboxylate-2,2′-biindolyl-3,3′-dicarboxaldehyde 11.** Into a 50-mL flame-dried round-bottom flask was placed the bis-indole **10** (200 mg, 0.694 mmol) followed by dry THF (20 mL), thus forming an insoluble suspension. Boc_2O (0.500 mL, 475 mg, 2.18 mmol) was then added in one portion followed by DMAP (21 mg, 0.17 mmol). The reaction was left to proceed under Ar for 10 min, during which time the solution became homogeneous. TLC of the reaction mixture indicated that the reaction was complete. The solvent was evaporated, and the crude material was purified by column chromatography (20% EtOAc/hexane), affording *N,N′*-di-*tert*-butyldicarboxylate-2,2′-biindolyl-3,3′-dicarboxaldehyde **11** as a white crystalline material (300 mg, 89%). mp > 170 °C dec; δ_H/ppm (300 MHz): 9.83 (2H, s), 8.44 (2H, d, J = 7.4 Hz), 8.33 (2H, d, J = 8.2 Hz), 7.55−7.44 (4H, m), 1.26 (18H, s); δ_C/ppm (75 MHz): 186.1, 148.6, 136.7, 136.2, 127.3, 125.3, 125.1, 123.4, 122.3, 115.6, 86.1, 27.6; ν_{max}/cm^{-1} (film): 2982, 1746, 1677, 1607, 1521, 1481, 1346, 1316; HRMS calcd for $C_{28}H_{28}N_2O_6$: 488.1947, found: 488.1916; MS: *m/z* 488 (M^+, 40%), 359 (27), 303 (85), 288 (78), 259 (100), 232 (24), 57 (99).

***N,N′*-Di-*tert*-butyldicarboxylate-2,2′-biindolyl-3,3′-divinyl 12.** Into a 50-mL two-necked oven-dried flask, fitted with a dropping funnel, was placed $MePPh_3Br$ (533 mg, 1.49 mmol), and the contents of the flask were blanketed with Ar. THF (10 mL) was added, forming a white suspension, and after cooling to −50 °C, *n*BuLi (1.2 M, 1.2 mL, 1.4 mmol) was added, resulting in a yellow solution with a white suspension. The reaction was allowed to proceed under Ar for 30 min at −50 °C and was then warmed to 0 °C for 10 min. The reaction was again cooled to −30 °C, and the bis-indole **11** (300 mg, 0.614 mmol) in THF (15 mL) was added dropwise over 5 min. The reaction was left to proceed for 18 h at 0 °C before the reaction mixture was poured onto water/crushed ice. The crude diene **12** was extracted into EtOAc and rapidly purified by column chromatography (5% EtOAc/hexane), affording the slightly impure diene **12** (as shown by NMR) as a yellow oil. δ_H/ppm (300 MHz): 8.40 (2H, d, J = 8.3 Hz), 7.92 (2H, d, J = 7.6 Hz), 7.43−7.31 (4H, m), 6.46 (2H, dd, J = 18.0 and 11.6 Hz), 5.75 (2H, dd, J = 18.0 and 1.1 Hz), 5.26 (2H, dd, J = 11.6 and 1.1 Hz), 1.14 (18H, s).

Di(*tert*-butyl)indolo[2,3-*a*]carbazole-11,12-dicarboxylate 13. Into a two-necked round-bottom flask fitted with a condenser (oven-dried and under Ar) was placed the diene **12** (assume 0.614 mmol) dissolved in toluene (60 mL). To the solution was added Grubbs II catalyst (26 mg, 0.031 mmol), and the solution was vacuum degassed before being covered by an Ar atmosphere. The solution was heated to 80 °C for 20 h, and then analysis of the reaction mixture by TLC indicated that not all the diene had reacted. More Grubbs II catalyst was added (14 mg, 0.016 mmol), and the reaction was left to proceed at 80 °C for another 4 h. The solvent was then evaporated in vacuo, and the crude material was purified by column chromatography (5−10% EtOAc/hexane). Recrystallization from an EtOAc/hexane mixture afforded the desired compound **13** as white crystals (178 mg, 64% or 74% if the recovered starting material is taken into account). mp > 230 °C dec; δ_H/ppm (300 MHz): 8.26 (2H, brd, J = 7.9 Hz), 8.03−7.99 (4H, m), 7.50−7.45 (2H, m), 7.40−7.35 (2H, m), 1.61 (18H, s); δ_C/ppm (75 MHz): 151.4, 139.8, 128.1, 127.3, 126.9, 126.7, 123.2, 119.5, 116.3, 115.4, 84.2, 28.3; ν_{max}/cm^{-1} (film): 2980, 1728, 1454, 1432, 1334, 1295, 1152; HRMS calcd for $C_{28}H_{28}N_2O_4$: 456.2049, found: 456.2011; MS: *m/z* 456 (M^+, 28%), 300 (64), 256 (100), 237 (6), 57 (41).

2-Acetyl-3-bromothiophene 15.[22b] Into a 100-mL three-neck round-bottom flask (dry, under Ar) was placed CH_2Cl_2 (15 mL), and the solvent was cooled using an ice bath before $AlCl_3$ (2.45 g, 18.4 mmol) was added. Partial dissolution of the $AlCl_3$ was observed. A dropping funnel was charged with freshly distilled acetyl chloride (1.34 mL, 1.48 g, 19.6 mmol) in CH_2Cl_2 (15 mL), and this was added over a 10-min period to the $AlCl_3$ suspension. After about 30 min of being stirred at 0 °C most of the $AlCl_3$ had dissolved. A second dropping funnel was charged with 3-bromothiophene (0.574 mL, 1.00 g, 6.13 mmol) in CH_2Cl_2 (15 mL), and this was added to the reaction mixture over a 10-min period. The reaction was left to proceed at 0 °C for 30 min and then warmed slowly to room temperature for another hour. Then the reaction mixture was cooled to 0 °C once again, and water (40 mL) was added carefully. After being transferred to a separating funnel, the reaction mixture was diluted with more CH_2Cl_2 (150 mL) and another portion of water (150 mL) was added. After being thoroughly mixed, the water layer was extracted twice with CH_2Cl_2, and the combined organic extracts were washed with saturated $NaHCO_3$ (100 mL), then brine (100 mL) and finally dried over anhydrous $MgSO_4$. Evaporation of the solvent and purification by column chromatography (5% EtOAc/hexane) followed by bulb−bulb distillation (130 °C at 10 mbar) afforded the desired compound as a white waxy solid (1.23 g, 98%). δ_H/ppm (300 MHz): 7.52 (1H, d, J = 5.2 Hz), 7.11 (1H, d, J = 5.2 Hz), 2.70 (3H, s); δ_C/ppm (75 MHz): 190.1, 139.1, 133.6, 132.2, 114.3, 29.6; ν_{max}/cm^{-1}: 1658, 1492, 1405, 1359, 1254; HRMS calcd for C_6H_5BrOS: 203.9244, found: 203.92506; MS: *m/z* 204 (M^+, 57%), 189 (99), 82 (22).

***tert*-Butyl 2-(2-Acetyl-3-thienyl)-1*H*-indole-1-carboxylate 16.** Into 50-mL two-necked round-bottom flask fitted with a dropping funnel and a condenser was placed $Pd(PPh_3)_4$ (1.12 g, 0.969 mmol) followed by 1-(*tert*-butoxycarbonyl)-1*H*-indol-2-yl-2-boronic acid **14** (1.90 g, 7.28 mmol), and the flask was degassed and refilled with Ar five times. The dropping funnel was then fitted with a pasteur pipet attached to an Ar line to act as a bubbler for the purposes of degassing the subsequent solvents. DME (12 mL) was added to the dropping funnel followed by 3-bromo-2-acetylthiophene **15** (1.00 g, 4.88 mmol), and the mixture was degassed for 10 min by gently bubbling Ar through the solution. This solution was then added to the flask in one portion, and the dropping funnel was charged with an aqueous Na_2CO_3 solution (2.00 M, 2.59 g, 24.5 mmol). This solution was similarly degassed before being added to the flask in one portion. The reaction mixture was then heated to reflux, and after about 1 h the solution became homogeneous and was pale orange in color. The mixture was heated at reflux for 3 d during which time a color change was observed from pale orange to light brown. Analysis of the reaction mixture indicated that the reaction had consumed nearly all of the thiophene **15** and that the desired compound **16** had formed as well as some of the deprotected analog **17**. After cooling, the reaction mixture was diluted with EtOAc (50 mL), water was added (50 mL), and the two phases were thoroughly mixed. The organic layer was separated, and the aqueous layer was extracted twice with EtOAc (2 × 50 mL). The combined organic fractions were washed with brine (100 mL) and dried over anhydrous $MgSO_4$. After removal of the solvent in vacuo, the crude mixture was taken up in THF (50 mL) and treated with Boc_2O (2.20 mL, 2.09 g, 9.58 mmol) and DMAP (90 mg, 0.74 mmol) for 2 h, thus converting trace amounts of the deprotected indole **17** back to the desired **16** (**17** and **15** have almost identical R_f values and so for purification purposes it is desirable to convert all **17** back to **16**). The reaction mixture was then diluted with EtOAc (50 mL) and water (50 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic fractions were washed with brine (100 mL) and dried over anhydrous $MgSO_4$. Evaporation of the solvent in vacuo and purification by column chromatography (5−10% EtOAc/hexane) afforded the desired *tert*-butyl 2-(2-acetylthiophen-3-yl)-1*H*-indole-1-carboxylate **16** (1.299 g, 78%) as a pale yellow solid. mp 92−94 °C; δ_H/ppm (300 MHz): 8.29 (1H, d, J = 8.3 Hz), 7.57−7.53 (2H, m), 7.39−7.36 (1H, m), 7.34−7.24 (1H, m), 7.07 (1H, d, J = 5.0 Hz), 6.58 (1H, s), 2.19 (3H, s), 1.34

(9H, s); δ_C/ppm (75 MHz): 191.0, 149.5, 141.3, 138.3, 136.7, 132.4, 132.0, 130.4, 128.7, 124.8, 123.0, 120.5, 115.6, 111.0, 83.5, 28.0, 27.5; ν_{max}/cm^{-1} (film): 2980, 1733, 1655, 1453, 1369, 1333, 1221, 1161; HRMS calcd for $C_{19}H_{19}NO_3S$: 341.1086, found: 341.1057; MS: *m/z* 341 (M^+, 27%), 241 (100), 226 (16), 57 (48).

2-(2-Acetyl-3-thienyl)-1*H*-indole 17. Method 1: Using $AlCl_3$. Into a dry 100-mL round-bottom flask under Ar was placed *tert*-butyl 2-(2-acetylthiophen-3-yl)-1*H*-indole-1-carboxylate **16** (1.00 g, 2.93 mmol) followed by dry CH_2Cl_2 (50 mL). The solution was cooled by means of an ice bath, and then $AlCl_3$ (508 mg, 3.81 mmol) was added in one portion. A color change from pale yellow to bright red occurred over a period of 15 min. The reaction was left to proceed at 0 °C for 1 h and then was quenched by the careful addition of water (50 mL). The reaction mixture was then diluted with CH_2Cl_2 (100 mL) and water (100 mL), and the phases were thoroughly mixed. The organic phase was separated, and the aqueous phase was extracted three times with CH_2Cl_2 (3 × 50 mL). The combined organic fractions were washed with brine (100 mL) and, after separation, dried over anhydrous $MgSO_4$. Evaporation of the solvent in vacuo and purification by column chromatography (5−10% EtOAc/hexane) afforded the desired product **17** as a bright yellow solid (612 mg, 87%).

Method 2: Using Microwave and SiO_2. Into a 250-mL round-bottom flask was placed *tert*-butyl 2-(2-acetylthiophen-3-yl)-1*H*-indole-1-carboxylate **16** (3.329 g, 9.750 mmol) followed by EtOAc (150 mL) and silica gel (150 g). The solvent was removed in vacuo, thus adsorbing the compound onto the silica gel, and trace amounts of solvent were removed under vacuum for 1 h. The adsorbate was then placed into a conventional microwave (500 W) for 30-s bursts with 2 min of cooling between each burst. After each burst, the adsorbate was mixed to ensure that the reaction progressed evenly through the adsorbate, and a small sample was removed for analysis by TLC (a small amount of the silica was placed into EtOAc to dissolve the adsorbed material, and this was analyzed by TLC). As the reaction progressed, the silica gel changed color from off-white to bright yellow. In this particular case, 7 × 45 s bursts were required to complete the reaction. Once the reaction was complete, the adsorbed product was loaded onto a column and purified by column chromatography (5−10% EtOAc/hexane). Evaporation of volatiles in vacuo afforded **17** as a bright yellow solid (2.335 g, 99%). mp 102−104 °C; δ_H/ppm (300 MHz): 12.29 (1H, brs), 7.69 (1H, d, J = 5.3 Hz), 7.62 (1H, d, J = 7.9 Hz), 7.53 (1H, d, J = 5.3 Hz), 7.49 (1H, d, J = 8.2 Hz), 7.26−7.21 (1H, m), 7.13−7.08 (1H, m), 6.96 (1H, brs), 2.70 (3H, s); δ_C/ppm (75 MHz): 192.1, 138.7, 136.0, 133.0, 132.4, 131.0, 130.7, 128.1, 123.3, 120.7, 120.1, 112.1, 103.9, 30.4; ν_{max}/cm^{-1} (film): 3178, 3119, 3055, 1645, 1611, 1570, 1537, 1487, 1405, 1377, 1220; HRMS calcd for $C_{14}H_{11}NOS$: 241.0561, found: 241.0564; MS: *m/z* 241 (M^+, 100%), 226 (26), 224 (12), 198 (12), 171 (10), 154 (8), 121 (9), 89 (5).

***tert*-Butyl 2-(2-Acetyl-3-thienyl)-3-formyl-1*H*-indole-1-carboxylate 18.** Into a two-necked 250-mL round-bottom flask fitted with a dropping funnel (dried and under Ar) was placed DMF (5.80 mL, 5.48 g, 74.9 mmol). The flask was then cooled by means of an ice bath, and $POCl_3$ (1.15 mL, 1.92 g, 12.5 mmol) was added dropwise by syringe. The formation of the Vilsmeier salt was allowed to proceed for 30 min under Ar at 0 °C. The dropping funnel was then charged with CH_2Cl_2 (100 mL), and this was added over a 10-min period to dilute the newly formed reagent. This solution was left to cool to 0 °C for another 15 min. Meanwhile, the dropping funnel was once again charged with CH_2Cl_2 (50 mL) and the indole **17** (2.15 g, 8.91 mmol). This yellow solution was then added dropwise over a period of 5−10 min to the flask still at 0 °C. After the addition was complete, the reaction was carefully monitored by TLC (every 5 min), and after about 15 min all of the starting material had been converted to the salt (only a highly UV active spot on the baseline if the TLC was run in 40% EtOAc/hexane). The reaction was immediately quenched by the careful addition of cold water (50 mL) and transferred to a 500-mL beaker. CH_2Cl_2 was added to dilute the mixture (100 mL), followed by water (100 mL), and the mixture was stirred vigorously. By means of gentle heating, the two-phase mixture was warmed to the boiling point of the CH_2Cl_2, and then an aqueous 1 M NaOH solution was slowly added until the pH of the solution remained slightly basic. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 80 mL). The combined organic fractions were washed with brine (100 mL), separated, and dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent in vacuo afforded the crude intermediate, 2-(2-acetylthiophen-3-yl)-1*H*-indole-3-carbaldehyde, as a dark red solid. This crude material was taken up in dry THF (200 mL) and transferred to a dry 250-mL round-bottom flask under Ar. To the flask at room temperature was added Boc_2O (3.30 mL, 3.14 g, 14.4 mmol) followed by DMAP (0.122 g, 0.998 mmol), and the reaction was left to proceed for 18 h under Ar before being transferred to a separating funnel. Water (200 mL) was added, followed by EtOAc (200 mL), and after vigorous shaking the organic phase was separated. The aqueous phase was extracted with EtOAc (3 × 100 mL), and the combined organic fractions were washed with brine, separated, and dried over anhydrous $MgSO_4$. After filtration and evaporation of the solvent in vacuo, the crude product was obtained as a brown solid. Column chromatography (20−40% EtOAc/hexane) followed by recrystallization from EtOAc/hexane afforded the desired product **18** as an off-white solid (1.64 g, 50% over two steps). mp 139−140 °C (EtOAc/hexane); δ_H/ppm (300 MHz): 9.65 (1H, s), 8.36 (1H, d, J = 7.2 Hz), 8.25 (1H, d, J = 8.3 Hz), 7.68 (1H, d, J = 5.0 Hz), 7.48−7.38 (2H, m), 7.20 (1H, d, J = 5.0 Hz), 2.31 (3H, s), 1.37 (9H, s); δ_C/ppm (75 MHz): 189.4, 186.6, 148.8, 143.0, 141.7, 136.3, 134.1, 132.3, 130.6, 126.2, 125.3, 124.8, 121.9, 120.4, 115.3, 85.0, 28.4, 27.5; ν_{max}/cm^{-1} (film): 3103, 2981, 2821, 1745, 1669, 1607, 1571, 1454, 1317, 1228, 1153, 1134; HRMS calcd for $C_{20}H_{19}NO_4S$: 369.1035, found: 369.1029; MS: *m/z* 369 (M^+, 10%), 340 (13), 326 (22), 269 (17), 254 (14), 240 (72), 226 (100), 57 (91), 41 (16).

***tert*-Butyl 4-Methyl-10*H*-thieno[3,2-*a*]carbazole-10-carboxylate 20.** Into a 50-mL two-necked round-bottom flask (oven dried, under Ar) was placed $MePPh_3Br$ (2.90 g, 8.12 mmol) followed by dry Et_2O (30 mL). The white suspension was cooled to −10 °C, and then *n*BuLi (1.4 M, 5.8 mL, 8.1 mmol) was added dropwise, thus forming a yellow solution. The solution was allowed to warm to room temperature and stirred for another 1.5 h. Stirring was stopped, and the white salt was allowed to settle, leaving a yellow solution. Into a separate 100-mL round-bottom flask fitted with a dropping funnel (oven dried, under Ar) was placed the dicarbonyl **18** (300 mg, 0.812 mmol) followed by dry Et_2O (60 mL), and the solution was cooled to 0 °C by means of an ice bath. The ylide solution from the first flask was transferred by cannula into the second flask containing the dicarbonyl **18** in Et_2O over a 10-min period. The reaction mixture was stirred for 30 min at 0 °C and then quenched by the addition of water (60 mL). The Et_2O layer was separated, washed successively with water (2 × 100 mL), then brine (100 mL). After drying the Et_2O layer with $MgSO_4$, the crude intermediate diene was adsorbed onto silica gel and purified hastily by column chromatography. The diene, now suspended in EtOAc/hexane, was then concentrated by removing 80% of the solvent mixture in vacuo, and then toluene was added (150 mL), and the mixture was again concentrated in vacuo to about 80% of its original volume. Toluene (150 mL) was added once again, and the volume was reduced in vacuo to 20 cm^3, thus removing most of the EtOAc/hexane without ever fully concentrating the diene (which is unstable when neat). The solution was transferred to a 50-mL round-bottom flask, degassed several times in vacuo, and then Grubbs II catalyst was added (50 mg, 0.059 mmol). After degassing once more, the flask was covered in aluminum foil, and the reaction was allowed to proceed under Ar at room temperature for 3 h. Analysis of the reaction mixture by TLC

indicated that not all of the diene had reacted, and therefore a further quantity of Grubbs II catalyst was added (30 mg, 0.035 mmol), and the reaction mixture was degassed again and left for 18 h. The solvent was then removed in vacuo, and the crude material was purified by column chromatography to afford the desired product **20** as a white solid (109 mg, 40% over two steps). mp 111−115 °C; δ_H/ppm (300 MHz): 8.17−8.12 (2H, m), 7.95 (1H, d, J = 7.4 Hz), 7.70 (1H, s), 7.47 (1H, d, J = 5.7 Hz), 7.44−7.42 (1H, m), 7.39−7.31 (1H, m), 2.67 (3H, s), 1.76 (9H, s); δ_C/ppm (75 MHz): 151.2, 141.2, 138.4, 132.2, 127.7, 127.2, 126.3, 126.0, 125.9, 123.9, 123.3, 122.9, 119.1, 115.8, 115.7, 84.2, 28.3, 20.5; ν_{max}/cm^{-1} (film): 2978, 2932, 1732, 1595, 1471, 1452, 1428, 1365, 1316, 1295, 1240, 1154; HRMS calcd for $C_{20}H_{19}NO_2S$: 337.1136, found: 337.1138; MS: *m/z* 337 (M^+, 39%), 281 (96), 237 (100), 118 (6), 57 (54), 41 (11).

4-Methyl-10*H*-thieno[3,2-*a*]carbazole 21. The carbazole **20** (93 mg, 0.28 mmol) in dry CH_2Cl_2 (15 mL) was treated at room temperature with TFA (0.63 mL, 93 mg, 0.82 mmol). The reaction mixture was then heated to reflux for 2 h, and after this time analysis of the reaction mixture by TLC indicated that not all of the starting material had reacted. Another addition of TFA was made (0.63 mL, 93 mg, 0.82 mmol), and after another hour of stirring the reaction mixture at room temperature the reaction was complete. The reaction mixture was then diluted with CH_2Cl_2 (30 mL) and washed with water (50 mL) before the two layers were separated. The water layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic extracts were washed with brine (100 mL) and then dried over anhydrous $MgSO_4$. Purification of the product by column chromatography afforded 4-methyl-10*H*-thieno[3,2-*a*]-carbazole **21** as a white solid (48 mg, 72%). mp 189−191 °C δ_H/ppm (300 MHz): 8.39 (1H, brs), 8.09 (1H, d, J = 7.8, Hz), 7.84 (1H, s), 7.63 (1H, d, J = 5.5 Hz), 7.54 (1H, d, J = 5.5 Hz), 7.51 (1H, d, J = 8.2 Hz), 7.49−7.38 (1H, m), 7.29−7.25 (1H, m), 2.71 (3H, s); δ_c/ppm (75 MHz): 139.2, 138.6, 132.9, 125.4, 124.8, 124.1, 123.9, 123.3, 119.9, 119.9, 119.7, 119.6, 116.8, 110.9, 20.5; ν_{max}/cm^{-1} (film): 3413 (NH str), 1609, 1452, 1360, 1249; HRMS calcd for $C_{15}H_{11}NS$: 237.0612, found: 237.0606; MS: *m/z* 237 (M^+, 100%), 204 (5), 191 (3), 118.5 (17).

2-Acetyl-3-bromofuran. Into a 100-mL three-neck round-bottom flask, under N_2, fitted with two dropping funnels was placed CH_2Cl_2 (15 mL), and the solvent was cooled by means of an ice bath. $AlCl_3$ (1.355 g, 10.16 mmol) was added in one portion, and the solution was stirred at 0 °C for 15 min, during which time partial dissolution of the $AlCl_3$ took place. A dropping funnel was charged with more CH_2Cl_2 (15 mL) and freshly distilled acetyl chloride (0.750 mL, 828 mg, 11.0 mmol). The acetyl chloride solution was then added over a 5-min period to the $AlCl_3$ solution, and the reaction was left to proceed at 0 °C for 30 min. During this time, complete dissolution of the $AlCl_3$ occurred. The second dropping funnel was charged with CH_2Cl_2 (15 mL) and 3-bromofuran (0.310 mL, 507 mg, 3.45 mmol), and this was added over a 5-min period to the reaction mixture, still at ice bath temperature. The reaction was left to proceed for 20 min and then allowed to warm to room temperature over a 10-min period. After cooling once again using an ice bath, water (50 mL) was added slowly, and then the reaction mixture was decanted to a dropping funnel before being diluted by the addition of CH_2Cl_2 (150 mL) and water (200 mL). After thoroughly mixing the phases, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic fractions were washed with saturated $NaHCO_3$ solution (200 mL), followed by brine (200 mL). After the organic layer was dried over anhydrous $MgSO_4$, the solvent was evaporated in vacuo. The crude product was then purified by column chromatography (5% EtOAc/hexane) followed by distillation (approx 120 °C, 10 mbar) to afford the desired compound as a white waxy solid (561 mg, 86%). δ_H/ppm: (300 MHz): 7.50 (1H, d, J = 1.7 Hz), 6.63 (1H, d, J = 1.7, Hz), 2.55 (3H, s); δ_C/ppm (75 MHz): 186.4, 148.3, 145.3, 117.4, 106.9, 27.4.

***tert*-Butyl 2-(2-acetylfuran-3-yl)-1*H*-indole-1-carboxylate 22.** Into a two-neck round-bottom flask fitted with a dropping funnel and a condenser was placed $Pd(PPh_3)_4$ (1.73 g, 1.50 mmol), and the reaction vessel was degassed and refilled with Ar gas five times. The dropping funnel was charged with DME (28 mL) and 1-(*tert*-butoxycarbonyl)-1*H*-indol-2-yl-2-boronic acid **14** (2.90 g, 11.1 mmol). Ar gas was then bubbled into the dropping funnel by means of a pasteur pipet, and dissolution of the boronic acid occurred almost immediately. During this period of degassing, 2-acetyl-3-bromofuran (1.20 g, 6.34 mmol) was added to the dropping funnel and degassing was continued for another 5 min. The solution was then discharged into the reaction vessel, and the dropping funnel was recharged with an aqueous Na_2CO_3 solution (2.0 M, 3.3 g, 31 mmol). This solution was similarly degassed for 10 min and then discharged into the reaction vessel. The two-phase mixture was heated and left to reflux for 3 d. During this time the solution became homogeneous, and a color change from yellow to pale brown occurred. The reaction mixture was cooled and decanted into a dropping funnel and then diluted with EtOAc (200 mL) and water (200 mL). After thorough mixing, the organic phase was separated, and the aqueous phase was extracted three times with EtOAc (3 × 100 mL). The combined organic fractions were then washed with brine (200 mL) and dried over anhydrous $MgSO_4$. After evaporation of the solvent in vacuo, the crude material was purified by column chromatography (5−10% EtOAc/hexane), affording the desired *tert*-butyl 2-(2-acetylfuran-3-yl)-1*H*-indole-1-carboxylate **22** (1.61 g, 78%) as well as a small amount of 2-(2-acetylfuran-3-yl)-1*H*-indole **23**. mp 98−99 °C; δ_H/ppm (300 MHz): 8.20 (1H, d, J = 8.4 Hz), 7.57 (1H, d, J = 1.6 Hz), 7.55 (1H, d, J = 7.9 Hz), 7.37−7.31 (1H, m), 7.27−7.21 (1H, m), 6.67 (1H, s), 6.61 (1H, d, J = 1.6 Hz), 2.37 (3H, s), 1.45 (9H, s); δ_C/ppm (75 MHz): 186.8, 149.6, 148.4, 144.1, 137.0, 130.0, 128.7, 125.6, 124.8, 122.8, 120.6, 115.4 (2×), 111.4, 85.5, 27.7, 26.9; ν_{max}/cm^{-1} (film): 3020, 1732, 1674, 1532, 1470, 1452, 1370, 1328, 1217; HRMS calcd for $C_{19}H_{19}NO_4$: 325.1314, found: 325.1296; MS: *m/z* 325 (M^+, 18%), 226 (15), 225 (100), 224 (31), 210 (8), 154 (10), 57 (49).

2-(2-Acetylfuran-3-yl)-1*H*-indole 23. Method 1: Using $AlCl_3$. Into a two-neck round-bottom flask under nitrogen was placed *tert*-butyl 2-(2-acetylfuran-3-yl)-1*H*-indole-1-carboxylate **22** (925 mg, 2.84 mmol) followed by CH_2Cl_2 (70 mL). After the solid had dissolved completely the flask was cooled by means of an ice bath, and then $AlCl_3$ (455 mg, 3.41 mmol) was added in one portion. The reaction was allowed to proceed for 2 h at 0 °C, during which time the color of the solution changed to bright red. The reaction was quenched by the careful addition of ice water, and the red color immediately disappeared. The reaction mixture was diluted with more CH_2Cl_2 (100 mL), followed by water (100 mL), and the phases were mixed and then separated. The aqueous phase was extracted three times with CH_2Cl_2 (3 × 50 mL), and the combined organic fractions were washed with brine and then dried over anhydrous $MgSO_4$. After filtration and evaporation of the solvent, the crude material was purified by column chromatography (5−20% EtOAc/hexane) to afford the desired product **23** as a bright yellow solid (536 mg, 84%).

Method 2: Using Microwave and SiO_2. The boc-protected indole **22** (500 mg, 1.54 mmol) was suspended in EtOAc (200 mL), and silica was added (200 g). The slurry was concentrated in vacuo until a dry off-white powder was obtained. This mixture was then placed into a conventional microwave (500 W) for 30-s bursts with 2 min of cooling between each burst. After each burst the adsorbate was mixed to ensure that the reaction progressed evenly through the adsorbate, and a small sample was removed for analysis by TLC (a small amount of the silica was placed into EtOAc to dissolve the adsorbed material and this was analyzed by TLC). In total, approximately 3 min of microwave heating was required to complete the reaction. As the reaction proceeded, the silica gradually became more yellow in color. Once the

reaction was complete, the adsorbed product was purified by column chromatography (5−10% EtOAc/hexane), affording **23** in 83% yield (288 mg) as a bright yellow solid. mp 137−138 °C; δ_H/ppm (300 MHz): 11.91 (1H, brs), 7.63 (1H, d, J = 7.9 Hz), 7.55 (1H, d, J = 1.6 Hz), 7.50 (1H, d, J = 8.2 Hz), 7.25 (1H, t, J = 7.1 Hz), 7.11 (1H, t, J = 7.4 Hz), 7.01 (1H, d, J = 1.6 Hz), 6.91 (1H, s), 2.66 (3H, s); δ_C/ppm (75 MHz): 189.7, 146.2, 145.8, 136.2, 128.9, 128.3, 126.9, 123.3, 120.6, 120.0, 112.4, 111.9, 103.4, 27.2; ν_{max}/cm^{-1} (film): 3253, 3019, 1656, 1573, 1523, 1475, 1397, 1360, 1250, 1216; HRMS calcd for $C_{14}H_{11}NO_2$: 225.0787, found: 225.0789; MS: *m/z* 225 (M^+, 100%), 224 (40), 210 (8), 196 (11), 182 (7), 154 (26).

***tert*-Butyl 2-(2-Acetylfuran-3-yl)-3-formyl-1*H*-indole-1-carboxylate 24.** Into a 100-mL two-neck round-bottom flask (dried, under Ar), fitted with a dropping funnel, was placed DMF (1.00 mL, 944 mg, 12.9 mmol), and the flask was cooled by means of an ice bath. $POCl_3$ (0.200 mL, 334 mg, 2.18 mmol) was added via a syringe, and the reaction was left to proceed for 10 min at 0 °C. By means of the dropping funnel, to the newly formed reagent was added CH_2Cl_2 (20 mL), and this solution was allowed to cool to 0 °C for 10 min. The dropping funnel was then charged with 2-(2-acetylfuran-3-yl)-1*H*-indole **23** (320 mg, 1.42 mmol) in dry CH_2Cl_2 (30 mL), and this was added dropwise over a period of 5 min. The reaction was left to proceed for another 5 min, and analysis of the reaction mixture by TLC indicated that all starting material had been converted to the Vilsmeier salt (only a highly UV active spot on the baseline if the TLC was run in 40% EtOAc/hexane). Ice cold water was immediately added (40 mL), and the reaction mixture was transferred to a beaker. CH_2Cl_2 was added (150 mL) followed by water (100 mL), and the two-phase mixture was stirred vigorously. By means of gentle heating the mixture was warmed to the boiling point of the CH_2Cl_2, and then 2 M NaOH solution was slowly added until the pH of the solution remained slightly basic. The organic phase was then separated, and the aqueous phase was extracted three times with CH_2Cl_2 (3 × 100 mL). The combined organic fractions were washed with brine (100 mL) and dried over anhydrous $MgSO_4$. Evaporation of the solvent afforded the crude product as a dark brown solid. Purification by column chromatography (40% EtOAc/hexane) removed most of the impurities; however, complete purification was not possible even after a second column. Recrystallization of the material (EtOAc/hexane mixtures) afforded the desired compound 2-(2-acetylfuran-3-yl)-1*H*-indole-3-carbaldehyde as pure (247 mg); however, by TLC it was clear that large amounts of the product were still in the mother liquor. ^{1}H NMR spectral data were then collected using the pure material, and then the pure and impure fractions were recombined and used in the next reaction. δ_H/ppm (300 MHz): 12.68 (1H, brs), 10.50 (1H, s), 8.29 (1H, d, J = 7.3 Hz), 7.67 (1H, d, J = 1.8 Hz), 7.59 (1H, d, J = 1.8 Hz), 7.51 (1H, dd, J = 1.3 and 6.9 Hz), 7.40−7.27 (2H, m), 2.70 (3H, s). The crude material (assume 1.42 mmol) was taken up in dry THF (40 mL), and Boc_2O was added in one portion (0.500 mL, 475 mg, 2.18 mmol) followed by DMAP (23 mg, 0.19 mmol). The reaction was left to proceed under Ar for 5 h at room temperature. Water was then added (50 mL), and the reaction mixture was diluted with EtOAc (100 mL). The organic phase was separated, and the aqueous phase was extracted three times with EtOAc (3 × 100 mL). The combined organic fractions were washed with brine (200 mL) and dried over anhydrous $MgSO_4$. After filtration and evaporation of the solvent in vacuo, the crude material was purified by column chromatography (20−30% EtOAc/hexane), followed by recrystallization from EtOAc/hexane mixtures to afford the desired *tert*-butyl 2-(2-acetylfuran-3-yl)-3-formyl-1*H*-indole-1-carboxylate **24** (397 mg, 79% over the two steps starting from **23**) as a pale yellow solid. mp 151−153 °C; δ_H/ppm (300 MHz): 9.82 (1H, s), 8.37−8.34 (1H, m), 8.20−8.17 (1H, m), 7.68 (1H, d, J = 1.7 Hz), 7.45−7.35 (2H, m), 6.72 (1H, d, J = 1.7 Hz), 2.45 (3H, s), 1.45 (9H, s); δ_C/ppm (75 MHz): 186.9, 186.7, 149.6, 148.9, 144.5, 140.0, 136.4, 126.2, 125.4, 124.7, 121.9, 121.0, 120.2, 116.4, 115.2, 85.1, 27.6, 26.6; ν_{max}/cm^{-1} (film): 2981, 1747, 1672, 1607, 1529, 1479, 1453, 1418, 1383, 1346, 1316, 1275, 1232; HRMS calcd for $C_{20}H_{19}NO_5$: 353.1263, found: 353.1269; MS: *m/z* 353 (M^+, 1%), 310 (10), 254 (29), 225 (13), 224 (26), 211 (16), 210 (100), 57 (67).

***tert*-Butyl-2a-methyl-1,2,2a,10c-tetrahydro-6*H*-cyclobuta[*c*]furo[3,2-*a*]carbazole-6-carboxylate 26. Part A.** Into a 250-mL two-neck round-bottomed flask under Ar was placed methyl triphenylphosphonium bromide (3.00 g, 8.40 mmol) followed by dry diethyl ether (150 mL). The phosphonium salt was not soluble in this solvent and thus formed a white suspension. The solution was cooled to 0 °C under Ar, and then *n*BuLi (1.4 M, 6.0 mL, 8.4 mmol) was added dropwise over a period of 5 min. The solution rapidly changed color to yellow as the *n*BuLi was added; however, a white solid remained insoluble in the solution (LiBr). After the addition of the *n*BuLi, the solution was stirred at 0 °C for 30 min and then warmed to room temperature for 30 min. Stirring was then stopped, and the insoluble LiBr salt was allowed to settle to the bottom of the flask.

Part B. Into a 250-mL two-neck round-bottom flask fitted with a dropping funnel was placed *tert*-butyl 2-(2-acetylfuran-3-yl)-3-formyl-1*H*-indole-1-carboxylate **24** (300 mg, 0.849 mmol) followed by diethyl ether (50 mL). The ylide as prepared in Part A was transferred by cannula into the dropping funnel. The contents of the round-bottom flask were cooled to 0 °C under Ar, and then the ylide was added in small portions (ca. 5−10 mL) until the formation of the diene was complete (as determined by monitoring the reaction by TLC). Without delay, the reaction was quenched by the addition of water (50 mL), and the mixture was diluted by the addition of EtOAc (100 mL). After the phases were thoroughly mixed, the organic phase was separated, and the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic fractions were collected, washed with brine (100 mL), and then dried over anhydrous $MgSO_4$. Without delay, the crude material was adsorbed onto silica and purified by column chromatography (5% EtOAc/hexane). The diene, now suspended in the EtOAc/hexane solvent, was then concentrated in vacuo to 80% of its original volume. Then toluene was added (100 mL), and the solution was once again concentrated to 80% of its original volume. Toluene was added once again (100 mL), and the solution was concentrated in vacuo to approximately 10 mL. In this way, the lower boiling solvents were essentially removed and replaced by toluene without ever fully concentrating the diene. The solution was then degassed in vacuo, and Grubbs II catalyst (72 mg, 0.085 mmol) was added. After 3 h analysis of the reaction mixture by TLC indicated that nothing appeared to be happening, and therefore the solution was heated to 80 °C overnight. Analysis of the reaction mixture by TLC still indicated that only starting material was present, and therefore another addition of Grubbs II catalyst was made (72 mg, 0.085 mmol), and the reaction was left to proceed at 80 °C for another 5 h. Analysis by TLC indicated no change, and therefore the mixture was adsorbed onto silica gel and purified by column chromatography (5% EtOAc/hexane), affording the unreacted diene as a clear oil (152 mg, 51% from dicarbonyl **24**). However, as soon as this oil was finally concentrated on the high vacuum, it rapidly changed color from clear to opaque and became waxy. After subjecting the wax for 3 h at room temperature to high vacuum the material was columned once again (5% EtOAc/hexane), affording *tert*-butyl 2a-methyl-1,2,2a,10c-tetrahydro-6*H*-cyclobuta[*c*]furo[3,2-*a*]carbazole-6-carboxylate **26** (82 mg, 28%, calculated from the dicarbonyl **24**) as a white waxy solid. δ_H/ppm (300 MHz): 7.98−7.92 (1H, m), 7.32 (1H, d, J = 1.9 Hz), 7.32−7.29 (1H, m), 7.21−7.15 (2H, m), 7.01 (1H, d, J = 1.9 Hz), 3.66 (1H, t, J = 7.5 Hz), 2.66−2.58 (1H, m), 2.46−2.36 (1H, m), 2.32−2.15 (2H, m), 1.72 (9H, s), 1.54 (3H, s); δ_C/ppm (75 MHz): 159.1, 150.5, 140.7, 136.2, 130.5, 128.5, 123.0, 122.7, 117.6, 116.0, 115.4, 111.8, 109.7, 84.0, 39.7, 39.7, 35.8, 28.3, 23.2, 26.2; ν_{max}/cm^{-1} (film): 2958, 1739, 1574, 1505, 1463, 1419, 1394, 1360,

1304, 1286, 1228; HRMS calcd for $C_{22}H_{23}NO_3$: 349.1678, found: 349.1684; MS: *m/z* 349 (M^+, 16%), 321 (5), 266 (18), 265 (100), 248 (4), 221 (55), 220 (23), 57 (30).

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Supporting Information Available: Copies of ^1H and ^{13}C NMR of **11**−**13**, **15**−**18**, **20**−**24**, **26**, and 2-acetyl-3-bromofuran and the ^1H NMR of 2-(2-acetylfuran-3-yl)-1*H*-indole-3-carbaldehyde. This material is available free of charge via the Internet at http://pubs.acs.org.

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