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Benzannulation reactions of Fischer carbene complexes for the synthesis of indolocarbazoles

Craig A. Merlic,* Ying You, Daniel M. McInnes, Andrea L. Zechman, Michael M. Miller and Qiaolin Deng

Department of Chemistry and Biochemistry, University of California, Los Angeles, CA 90095-1569, USA

Dedicated to Professor Barry M. Trost on the occasion of his 60th birthday

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Abstract—The synthesis of indolocarbazoles was achieved via photochemical and thermal annulation reactions of chromium Fischer carbene complexes. This methodology allows for facile incorporation of hydrogen bonding functionality which complements the pharmacophore contained within bioactive indolocarbazole natural products.

1. Introduction

The indolocarbazoles are natural products of medicinal and biochemical importance.[1] Their history dates back to 1977 with the isolation of staurosporine (**1**), initially named AM-2282, from *Streptomyces staurosporeus* by Omura and co-workers while searching for new microbial alkaloids present in actinomycetes.[2] The following year, the structure of **1** was established by X-ray crystallographic analysis to be comprised of a central indolocarbazole ring system linked by two *N*-glycosidic bonds to a lower carbohydrate moiety and an upper lactam ring (Fig. 1).[3] In addition to **1**, other indolocarbazoles were isolated soon thereafter including the arcyriaflavins (**3**) from the slime mold *Arcyria denudata*,[4] K-252a (**6a**) and K-252c (**4**) from *Nocardiopsis* strains K-252 and K-290, respectively,[5] and rebeccamycin (**8a**) from *Nocardia aerocoligenes*.[6] As indicated by the distinctive UV chromophore of these alkaloids, all possess the indolocarbazole backbone. In the subsequent years, many additional indolocarbazoles have been discovered.[7,8]

The indolocarbazole alkaloids are extremely interesting owing to the wide range of biological activities that they possess, including antimicrobial,[2] hypotensive,[9] and cell cytotoxic[10] activities, as well as inhibition of platelet aggregation.[11] The greatest interest in these compounds, however, has been due to their potent antitumor activity. Compounds containing the indolocarbazole core with one *N*-glycosidic bond, i.e. rebeccamycin, inhibit DNA topoisomerase I,[12] while those with two *N*-glycosidic bonds present, i.e. staurosporin, exhibit high levels of protein kinase C (PKC) inhibition.[10,13] A key structural feature of the heterochromatic aglycone is the presence of hydrogen bonding moieties at its top and bottom. Synthetic analogues containing labile hydrogen functionalities (i.e. –OH, $-CH_2OH$, $-NH_2$) on the imide nitrogen have been shown to possess enhanced inhibition of PKC and other biological activities.[14] Additional structure–activity relationship studies have revealed that the high potency of **1** is significantly reduced in the aglycon system (**4**).[15,16] Presently, several indolocarbazole alkaloids are in clinical trials for potential use in cancer therapy.[1d]

The novel structural features of these compounds and their significant biological relevance has prompted a flourish of activity from the synthetic community resulting in numerous studies directed towards the synthesis, as well as several disclosed total syntheses, of these natural products and their structural analogs (Fig. 2).[4,17–46] A number of interesting synthetic strategies were employed to prepare the indolocarbazole core in these syntheses. Most targeted construction of the central benzene ring, half used preformed indole units, and several utilized Diels–Alder reactions as the key step. Of particular note are the total syntheses of rebeccamycin and staurosporin, revealed by Clardy[22] and Danishefsky,[26] employing the reaction of 3,4-dibromo-*N*-methylmaleimide with indolylmagnesium halide, developed by Steglich,[4] to construct the main carbon skeleton. Through the use of a novel rhodium catalyzed carbenoid coupling to indole, Wood and co-workers[37] disclosed a common intermediate that led to the efficient synthesis of staurosporine and a number of its congeners. Van Vranken and coworkers[38]

Keywords: benzannulation; carbene complex; indolocarbazoles; palladium catalyzed cross-coupling.

* Corresponding author. Tel.: +1-310-825-5466; fax: +1-310-206-3722; e-mail: merlic@chem.ucla.edu

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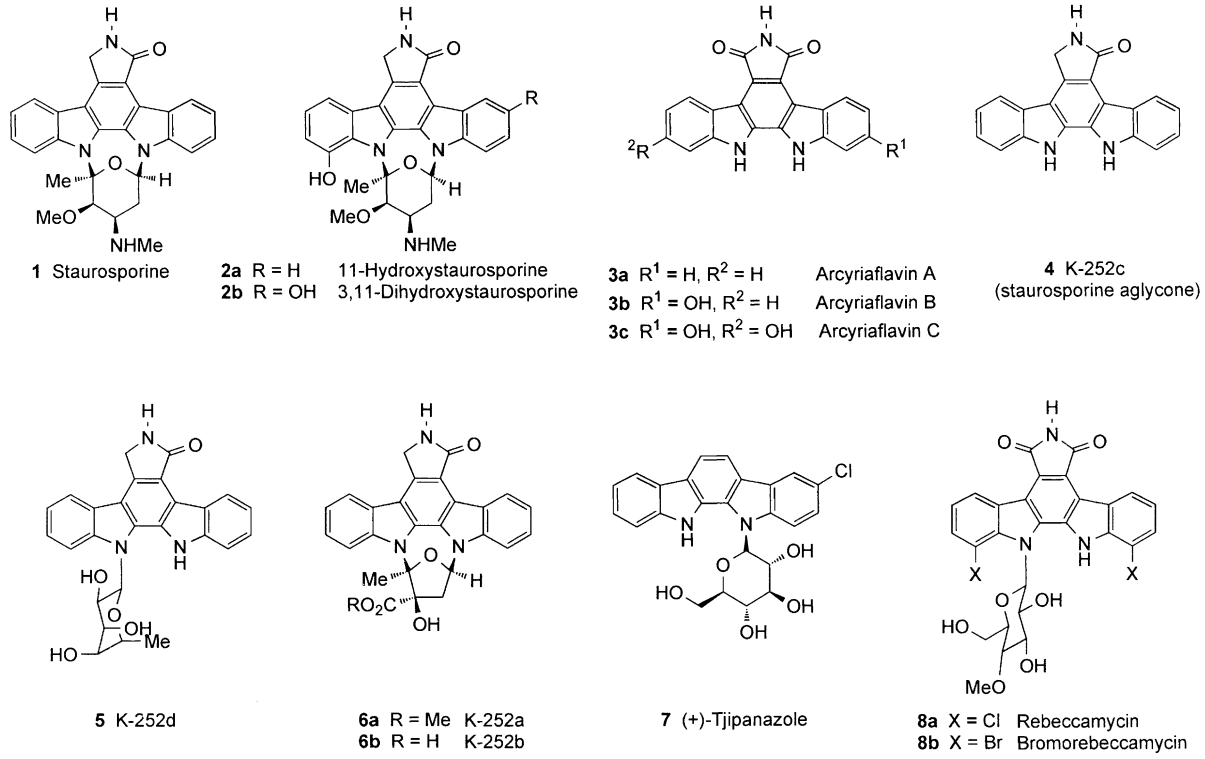
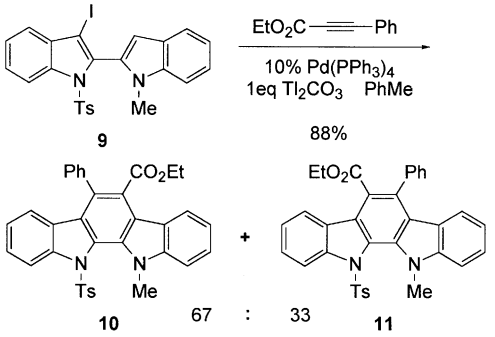


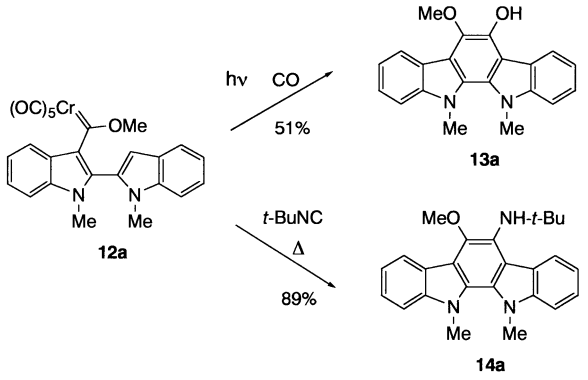
Figure 1. Representative indolocarbazoles.

elegantly demonstrated highly regioselective halogenation and glucosylation of Mannich cyclization products,[23c] allowing for the dissymmetric synthesis of several unsymmetrical rebeccamycin type indolocarbazoles. Other than Wood's route, the only other transition metal mediated procedure shown is that of Saulnier employing a novel double palladium catalyzed cyclization.[35]

We recently disclosed two alternative approaches to the indolocarbazole ring system through: (1) palladium catalyzed benzannulation reactions of biindolyl iodides and alkynes (Eq. (1)),[47] and (2) annulations of Fischer carbene intermediates (Eq. (2)).[48] Herein, we report a full account of our efforts in this arena expanding upon the latter strategy. This route provides access to a number of indolocarbazole cores containing new patterns of hydrogen bonding functionality on the central aryl ring which mimic or complement the pharmacophore contained within the bioactive indolocarbazole natural products.



(1)



(2)

2. Results and discussion

Our goal was to provide a short synthesis of the indolocarbazole core containing two orthogonal protecting groups to differentiate the indole nitrogens, as well as dissymmetric hydrogen bonding groups on the central benzene ring. The protecting groups could thus be removed and the indole nitrogens could consequently be selectively functionalized late in a synthesis installing the sugar moiety necessary in a total synthesis of the indolocarbazole natural products. Our strategy to form such differentially substituted indolocarbazoles centered on 2,2′-biindolyl intermediates, their conversion to Fischer chromium carbene complexes, and subsequent benzannulation reactions of these key complexes to establish the ABCEF ring system (Scheme 1), and thus the central core of the indolocarbazole alkaloids. The requisite 2,2′-biindolyl intermediates could arise by a variety of routes, but we eventually developed palladium

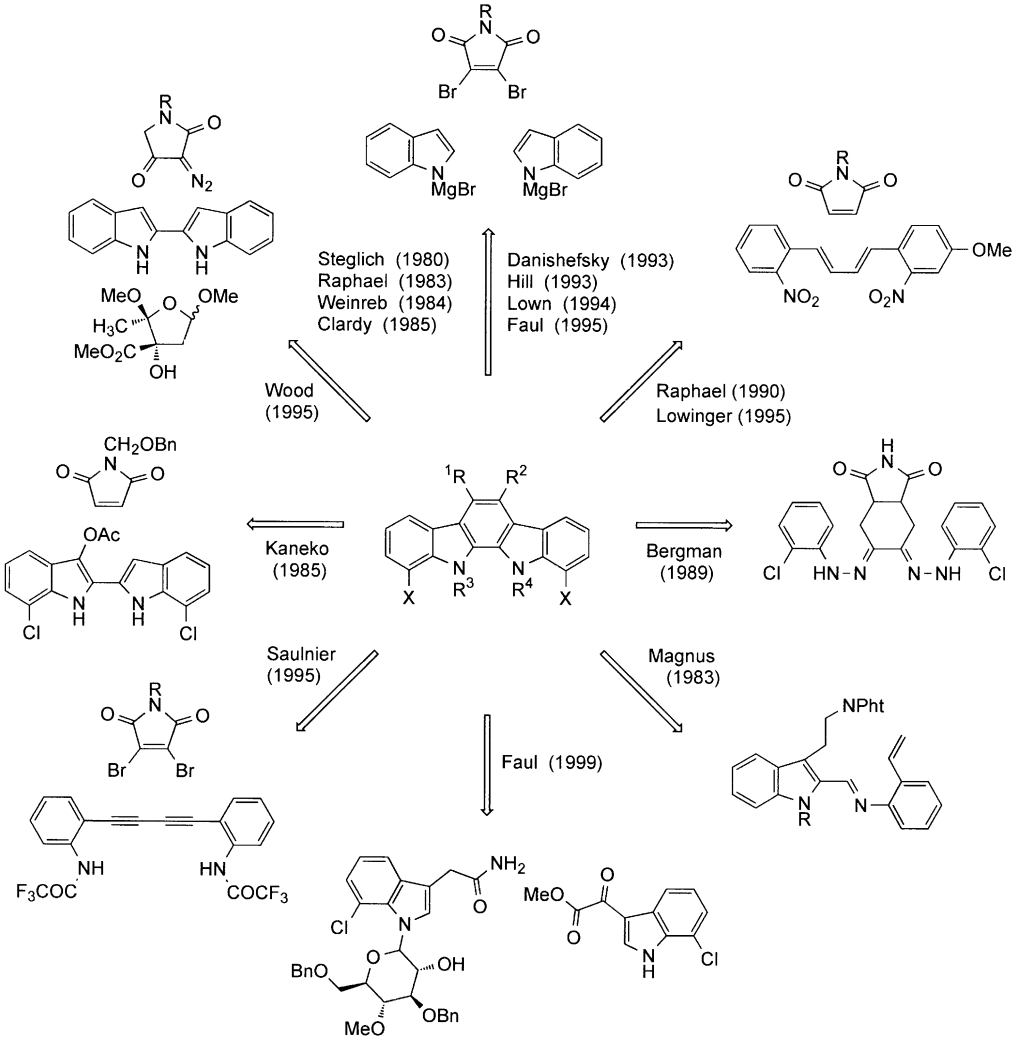
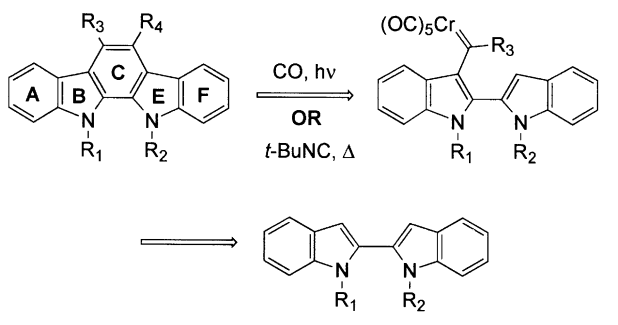


Figure 2. Approaches to indolocarbazole alkaloids.

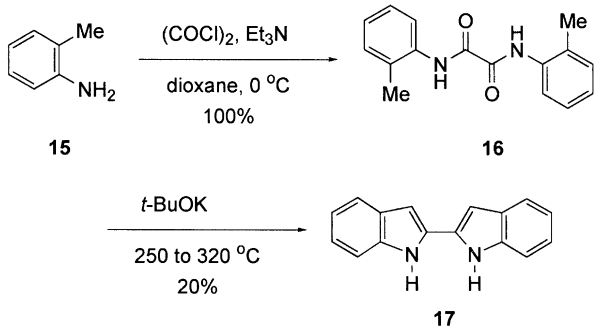
catalyzed cross-coupling of two indole substructures. This overall synthetic route demonstrates the utility of our previously reported Fischer carbene methodology, in which carbene complexes are converted into aromatic alcohols and amines.[49,50]

2.1. Approaches toward symmetrical 2,2′-biindolyls

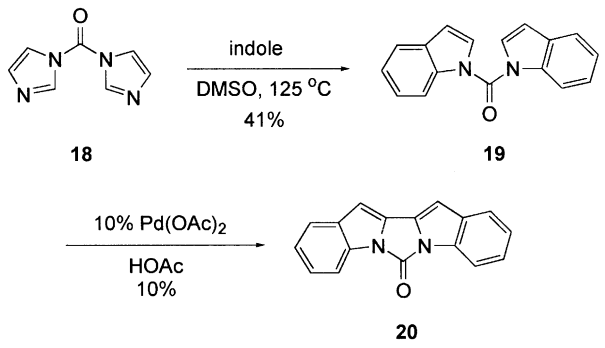
The first method for preparation of 2,2′-biindolyls explored involved a double Madelung cyclization reaction of *N*,*N*′-bis(*o*-tolyl)oxamide.[27] Oxalyl chloride was condensed with *ortho*-toluidene (**15**) according to the procedure of Wallace and co-workers to form *N*,*N*′-bis(*o*-tolyl)oxamide (**16**), in quantitative yields. The Madelung cyclization was then accomplished by heating **16** with freshly prepared potassium *tert*-butoxide to 250°C and then to 320°C (Scheme 2). Much decomposition occurred under these extreme conditions and yields of 2,2′-biindolyl (**17**) were typically on the order of 20%, though reactions at lower temperatures resulted in little or no product.[51]



Scheme 1. Synthetic design.



Scheme 2.

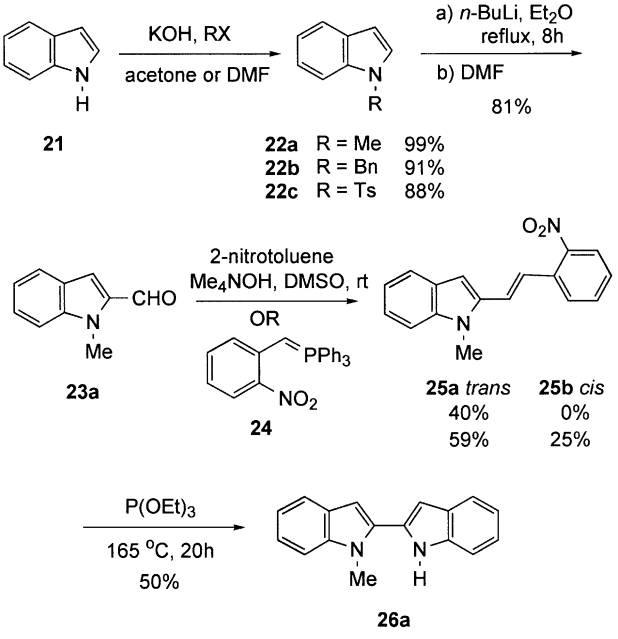


Scheme 3.

Due to the inefficient Madelung cyclization of **16** our next approach involved a palladium mediated coupling of the 2 and 2′ positions of 1,1′-carbonyldiindole (**19**) to form 1,1′-carbonyl-2,2′-biindolyl (**20**). Two major advantages of this route were foreseen: (1) the 2,2′-biindolyl core would be assembled without employing the problematic Madelung cyclization; and (2) ring opening with a nucleophilic organometallic reagent would lead directly to an unsymmetrical mono-protected 2,2′-biindolyl. As shown in Scheme 3, 1,1′-carbonyldiimidazole[52] was converted to *N*,*N*′-carbonyldiindole (**19**) in 41% yield using the procedure developed by Bergman.[53] The key coupling step provided the desired product in low yield and required stoichiometric amounts of palladium acetate, so it was deemed prohibitively expensive.[54] Addition of various co-oxidants (Ac_2O, MnO_2, and $Cu(OAc)_2$) in attempts to make the reaction catalytic in palladium resulted in no marked improvement in yield.

2.2. Nitrene cyclization approach to unsymmetrical 2,2′-biindolyls

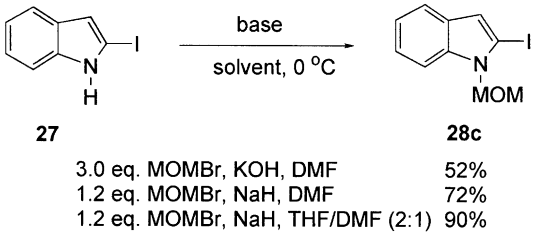
The next strategy employed the nitrene cyclization reaction of Cadogan[55] to build one indole ring, and resulted in a mono-protected 2,2′-biindolyl in modest yield (Scheme 4). *N*-alkylation or sulfonylation of indole took place in high yields using the procedure of Kikugawa.[56] Using the procedure of Hoffmann and co-workers,[57] formylation of the 2 position of *N*-methylindole (**22a**) was accomplished in 81% yield. Lower yields were obtained, however, when *N*-tosyl or *N*-benzyl indoles, **22b** and **22c**, were used and efforts to optimize the reaction using other formylation conditions were unsuccessful. Applying the methodology of Watanabe and coworkers,[58] condensation of *N*-methylindole-2-carboxaldehyde (**23a**) with 2-nitrotoluene resulted in indole substituted alkene **25a** in modest yield. A similar yield was observed for condensation with *N*-benzylindole-2-carboxaldehyde. Varying conditions such as solvent (DMF, THF) and base (KOMe, NaH) led to minimal product formation. A higher yielding route to the indole substituted alkene was achieved using a Wittig reaction.[59] Addition of *N*-methylindole-2-carboxaldehyde to a cold solution of ylide **24** resulted in 59% and 25% yields of *trans* and *cis* indole substituted alkenes **25**, respectively. Unfortunately, modest yields of the subsequent nitrene cyclization were achieved. Employing Cadogan's protocol,[55] cyclization of *trans*-alkene **25a** with triethylphosphite resulted in a 50% yield of **26a**. Due to the limitations in this strategy of modest yields, limits on structural diversity, and the number of steps, a more efficient and versatile synthetic route toward unsymmetrical 2,2′-biindolyls was devised.



Scheme 4.

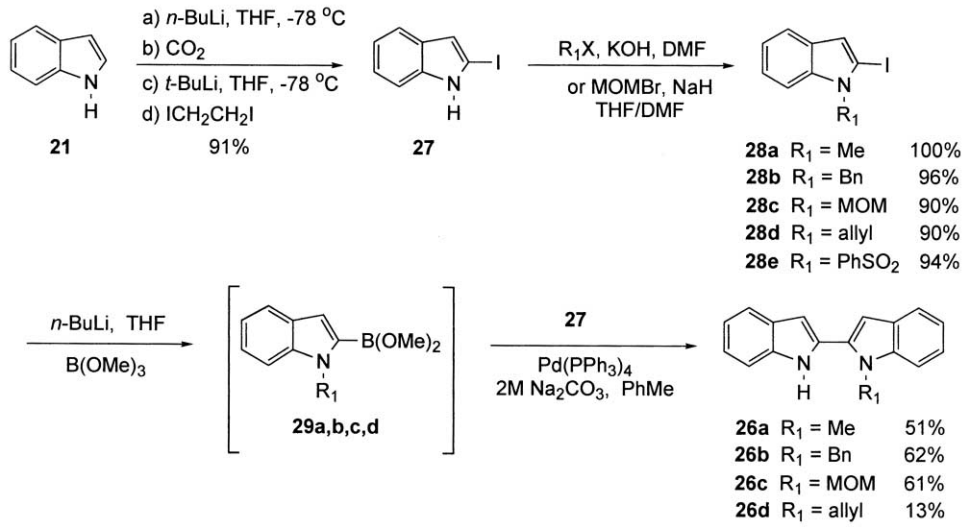
2.3. Palladium catalyzed cross-coupling approach to unsymmetrical 2,2′-biindolyls

Cross-coupling of two indole units under palladium catalysis turned out to be ideal for the preparation of unsymmetrical 2,2′-biindolyls as illustrated in Scheme 5.[60] Formation of 2-iodoindole (**27**) from indole using the method reported by Bergman proceeded in 91% yield.[61] *N*-Protection of 2-iodoindole with alkyl and sulfonyl groups proceeded in excellent yields. 2-Iodo-1-methoxymethylindole (**28c**) was initially prepared by a standard method for the synthesis of *N*-substituted 2-iodoindoles (KOH, DMF, 0°C; CH_3OCH_2Br), but this procedure requires a large excess of expensive methoxymethyl bromide with only modest product yields. In addition, difficulty arises in separating the product from excess starting material in large scale protocols due to similar R_f values of the two compounds. These obstacles were overcome by optimization of the reaction conditions using NaH and a mixed solvent system of 2:1 THF/DMF leading to excellent yields of the desired product (Eq. (3)).



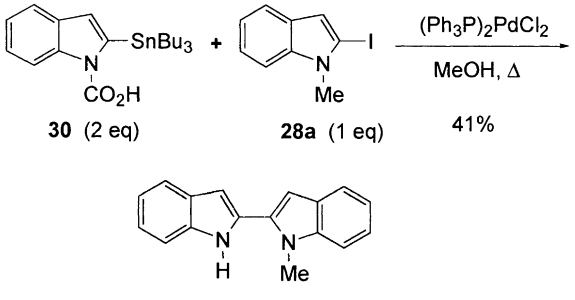
(3)

In the first palladium catalyzed cross-coupling reaction, *N*-methyl-2-iodoindole (**28a**) was converted into the boronic ester **29a**. Using modified Suzuki conditions, the in situ prepared **29a** was coupled with 2-iodoindole to afforded



Scheme 5. Palladium catalyzed biindolyl synthesis.

unsymmetrical 2,2′-biindolyl **26a** in 51% overall yield from **28a** (Scheme 5).[62] Side products included the homocoupling of **27**, as well as of **29a**. Several other palladium-catalyzed cross-coupling reactions were investigated in attempts to further improve the biindolyl preparation. Employing Hudkins' procedure,[63] the Stille cross-coupling reaction of organotin **30** and iodoindole **28a** produced biindolyl **26a** in 41% yield (Eq. (4)). In contrast, the Negishi method[64] led to the protonated product, 1-methylindole, which most likely arose from protonation of the zinc reagent by the unprotected 2-iodoindole coupling partner (Eq. (5)). Based on these results, the Suzuki method was utilized for the other biindolyls.



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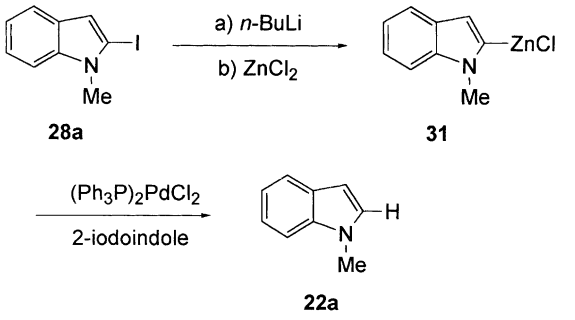
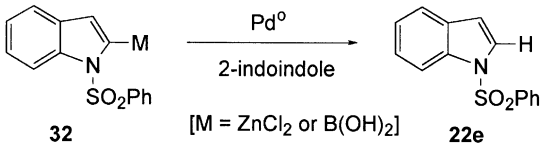


(5)

Due to the known difficulty in unmasking protected indoles, efforts were made to synthesize 2,2′-biindolyl systems with several different removable protecting groups (Scheme 5). *N*-Benzyl-2-iodoindole (**28b**) and *N*-methoxymethyl-2-iodoindole (**28c**) were successfully converted to the corresponding biindolyls **26b** and **26c** in 62% and 61% yields, respectively. *N*-allyl 2-iodoindole (**28d**) was coupled with 2-iodoindole to form 1-allyl-2-(indol-2′-yl)indole (**26d**) in low yield, with many side products being formed, possibly due to intra- or intermolecular Heck type reactions. Due to the problematic nature of the synthesis of **26d**, the reactivity of this compound was not investigated further. Attempts to couple either *N*-benzenesulfonylindol-2-yl boronic acid or the corresponding zinc chloride resulted in recovery of the protonated product, *N*-benzenesulfonylindole (**22e**) (Eq. (7)). In general, biindolyls **26** are easily visualized on TLC under UV light due to their very intense fluorescence.



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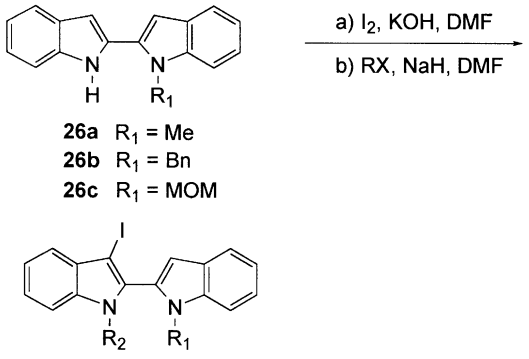


(7)

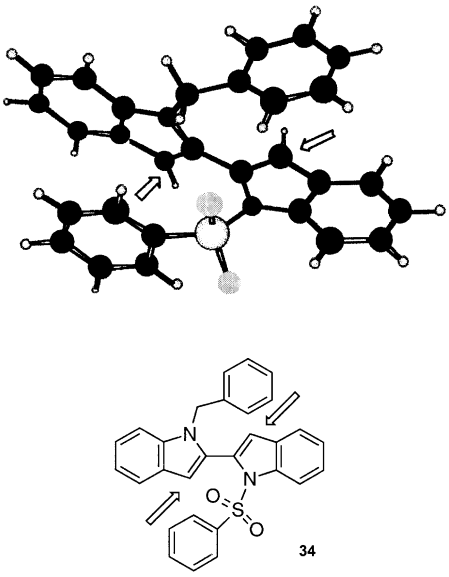
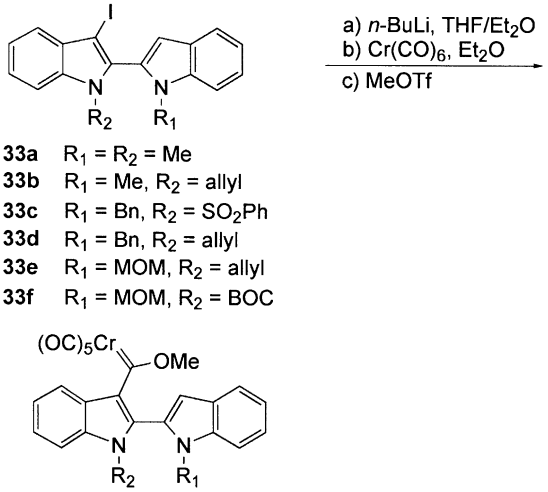


Figure 3. Most stable conformer of **34**.

2.4. Preparation of key chromium carbene complexes and subsequent benzannulation reactions

Chromium carbene precursors were prepared via iodination at the 3 position of biindolyls **26** using the procedure of Bocchi and Palla,[65] followed by *N*-protection (Eq. (7)). The resultant iodides **33** were formed in good to excellent yields. Hindered rotation about the 2–2′ bond was evident from the diastereotopic AB patterns in the ^{1}H NMR spectra for the protons in the methylene groups of **33b**, **33c**, **33d**, **33e**, and **33f**. Due to the presence of a heavy atom, iodides **33** do not fluoresce.[66]

Preparations of carbene complexes **12a** and **12b** were accomplished under the standard conditions of metal halogen exchange with *n*-butyllithium, addition to chromium hexacarbonyl and methylation with methyl triflate (Eq. (8)).[67] Both complexes were isolated as deep red solids with spectral signals typical of carbene complexes. However, differentially protected biindolyls **33c** and **33d** failed to yield the corresponding carbene complexes under such conditions and only methylated products were observed. Initially, we proposed that the electron withdrawing benzenesulfonyl protecting group in **33c** inductively stabilized an anion at the 3 position making it less nucleophilic and unable to add to the weakly electrophilic chromium hexacarbonyl. However, the failure using biindolyl **33d**, which possesses an allyl protecting group instead of a benzenesulfonyl protecting group rules out that possibility. These results then pointed to the possible role of sterics in limiting formation of carbene complexes. Nucleophilic addition to a carbonyl ligand in chromium hexacarbonyl is hindered by the presence of the four *cis* CO ligands which effectively create a 'wall' of steric hindrance, so smaller nucleophiles should be less problematic. Indeed, iodide **33e**, with small allyl and methoxymethyl nitrogen protecting groups, led smoothly to carbene complex **12e**. Surprisingly, iodide **33f**, with a large BOC protecting group, also successfully led to a carbene complex (**12f**). As with the starting iodides **33e** and **33f**, the methylene protons in the complexes were diastereotopic due to hindered rotation about the biaryl axis. In fact, spectral analysis of complex **12f** was quite complex due to additional hindered rotations, most likely about the C3 to carbene carbon bond as we have seen in previous systems.[49b]



33a	$R_1 = R_2 = Me$	
33b	$R_1 = Me$, $R_2 = allyl$	
33c	$R_1 = Bn$, $R_2 = SO_2Ph$	
33d	$R_1 = Bn$, $R_2 = allyl$	
33e	$R_1 = MOM$, $R_2 = allyl$	
33f	$R_1 = MOM$, $R_2 = BOC$	
12a	$R_1 = R_2 = Me$	55%
12b	$R_1 = Me$, $R_2 = allyl$	66%
12c	$R_1 = Bn$, $R_2 = SO_2Ph$	0%
12d	$R_1 = Bn$, $R_2 = allyl$	0%
12e	$R_1 = MOM$, $R_2 = allyl$	59%
12f	$R_1 = MOM$, $R_2 = BOC$	42%

(8)

To better understand the steric effects involved in these systems, a Monte Carlo conformational search was carried out with the AMBER force field in Macromodel on a series of substituted 2,2′-biindolyls.[68] Calculations indeed supported the claim that the difficulty encountered in generating the desired carbene intermediates was due to the sterically encumbering protecting groups. For example, with two large protecting groups, the preferred conformation of *N*-benzenesulfonyl-*N*′-benzyl-2,2′-biindolyl (**34**) has an N1–C2–C2′–N1′ dihedral angle of 72.8° (Fig. 3). The two indole planes are nearly perpendicular to one other and the aryl rings of the benzyl and benzenesulfonyl protecting groups π-stack with the opposite indole moieties with the distances between the benzene rings and indole moieties less than 4 Å. Because the protecting groups reach across to block the 3 position of the adjacent indole nucleus, bulky chromium hexacarbonyl may not be able to access either the C3 or C3′ positions in such a system, while small electrophiles such as methyl triflate may still react.

By substituting the benzenesulfonyl group of **34** with the smaller methoxymethyl protecting group, the N1–C2–C2′–N1′ dihedral angle in the preferred conformation of *N*-benzyl-*N*′-methoxymethyl-2,2′-biindolyl (**35**) increases to −103.1° (Fig. 4). π-Stacking interactions that block the C3′ position were again observed between the aryl ring of the benzyl group and the opposite indole moiety, thus providing a reasonable explanation why *N*′-benzyl-3-iodo-*N*-allyl-2,2′-biindolyl (**33d**) failed to produce the desired Fischer carbene complex. However, the C3 position is not predicted to be blocked by the MOM protecting group. Therefore, 3-iodo-2,2′-biindolyls with small protecting groups at the *N*′ position are predicted to be convertible to the corresponding

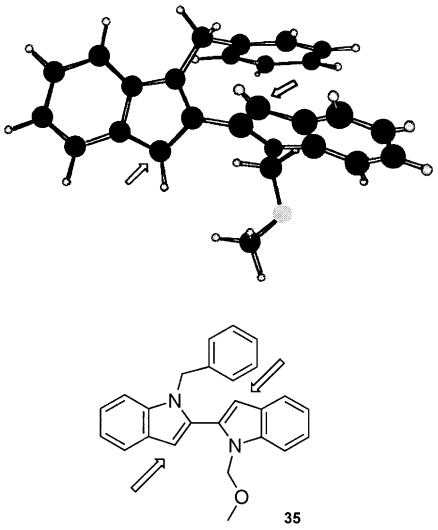


Figure 4. Most stable conformer of **35**.

Fischer carbene complex. Indeed, iodides **33e** and **33f** (with a large BOC group on the same ring) were successfully converted into carbene complexes **12e** and **12f**, respectively.

Benzannulation reactions of chromium carbene complexes **12a**, **12b**, **12e** and **12f** were employed to construct the central ring of the indolocarbazoles with concomitant formation of hydrogen bonding moieties (Scheme 6). Photolysis of **12a** generated the benzannulation product **13a** in 51% yield via the intermediacy of a photogenerated ketene, as previously reported from our group.[49a,b] Product formation was confirmed by the presence of two doublets at 8.22 and 8.37 ppm for the bay region protons in the ^{1}H NMR spectrum and the phenolic proton at 9.37 ppm. Complex **12a** also underwent an aminobenzannulation reaction[49c,d] via a thermal reaction with *tert*-butyl isonitrile to produce amine **14a** in 89% yield. Addition of *tert*-butyl isonitrile to the carbene complex generates an intermediate ketenimine complex that undergoes a thermal 6π electrocyclization reaction followed by tautomerization to yield the product amine. Again, the desired product was obvious from the bay region protons at 8.35 and 8.77 ppm in the ^{1}H NMR spectrum. Indolocarbazoles **13b** and **14b** were also obtained in good yields from the photochemical and thermal benzannulation reactions of carbene complex **12b**.

Finally, our focus turned to the cyclization reactions of carbene complexes **12e** and **12f**, which contain removable protecting groups (Scheme 6). In analogy to complexes **12a** and **12b**, both photochemical and isonitrile-initiated thermal annulation reactions were successful, generating products **13e** (63%) and **14e** (74%) from **12e** and **13f** (71%) and **14f** (68%) from **12f**. In fact, it seemed that the nature of the protecting groups did not exert a strong influence on the outcome of the benzannulation reactions. However, choice of solvent did play a significant role in some of the photochemical reactions. When toluene was used as the solvent, the cyclization product of **12e** was isolated in a substantially lower yield (14%) as compared to the reaction in THF (63%). Surprisingly, cyclization of **12f** in toluene proceeded in a 71% yield. In contrast to the corresponding precursor iodides and carbenes, diastereotopic AB patterns for the methylene protons were not observed in the ^{1}H NMR spectra for the benzannulation products.

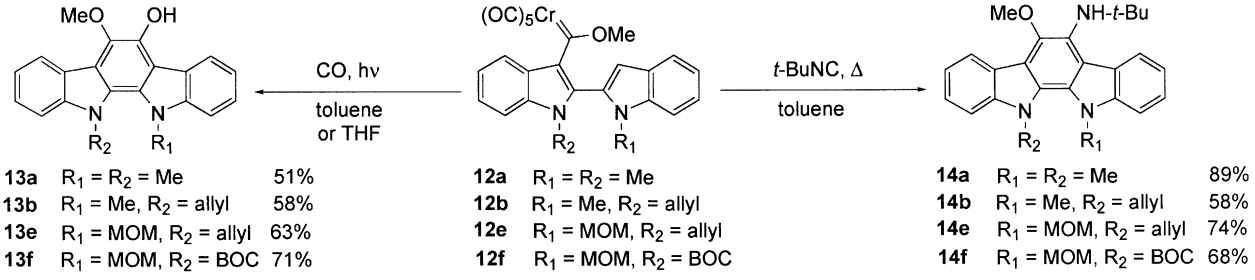
In summary, we have demonstrated that complex and sterically encumbered 2,2′-biindolyl chromium carbene complexes containing removable protecting groups can be prepared and subsequently employed in both thermal and photochemical annulation reactions. The differentially protected indolocarbazole nitrogens will allow for concise and selective glycoside formation in route to analogues of indolocarbazoles containing hydrogen bonding functionality complementing important protein kinase C inhibiting indolocarbazole natural products.

3. Experimental

3.1. General experimental procedures

All reactions were carried out in flame-dried glassware under a static argon or nitrogen atmosphere unless otherwise stated. Tetrahydrofuran (THF), dioxane, and diethyl ether were distilled from sodium-benzophenone ketyl; dichloromethane, acetonitrile, pyridine, and hexanes were distilled from calcium hydride. Reagents were obtained commercially and purified before use unless otherwise indicated. Flash column chromatography was performed employing the Still protocol.[69]

Infrared (IR) spectra were recorded on a Nicolet 510P FT-IR spectrophotometer and selected absorption maxima are reported in cm^{-1}. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were obtained with a Bruker AM 200 or AM 360 or ARX 400 or 500 spectrometer in deuteriochloroform ($CDCl_3$: δ 7.26 ppm for ^{1}H, δ 77.0 ppm for ^{13}C); benzene (C_6D_6: δ 7.16 ppm for ^{1}H, δ 128.39 ppm for ^{13}C); acetone



Scheme 6. Benzannulation reactions of Fischer carbene complexes.

($(CD_3)_2CO$: δ 2.05 ppm for ^1H, δ 29.92 ppm for ^{13}C); or dimethylsulfoxide ($(CD_3)_2SO$: δ 2.50 ppm for ^1H, δ 39.52 ppm for ^{13}C) solution. Chemical shifts are given in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broadened). Coupling constants, *J*, are reported in Hertz. Mass spectra were obtained on either an AEI MS902 spectrometer with an ionization voltage of 70 eV or a VG ZAB-SE spectrometer.

3.1.1. 1-Benzyl-2-iodoindole (28b). 2-Iodoindole (800 mg, 3.29 mmol) was dissolved in DMF (10 mL) and the solution was cooled to 0°C. Powdered KOH (277 mg, 4.94 mmol) was added and the mixture stirred for 5 min at 0°C. Benzyl bromide (619 mg, 362 mmol) was added dropwise to the reaction mixture. After 5 min, the reaction mixture was diluted with Et_2O and washed with saturated NaCl solution. The organic layer was dried ($MgSO_4$) and the solvent was removed in vacuo to yield 1.10 g (96%) of 1-benzyl-2-iodoindole (**28b**) as a white solid after chromatography (95:5 hexane/EtOAc).

^1H NMR (360 MHz, $CDCl_3$) δ: 5.42 (2H, s), 6.88 (1H, s), 7.04–7.11 (4H, m), 7.23–7.30 (4H, m), 7.55–7.58 (1H, m). ^{13}C NMR (90 MHz, $CDCl_3$) δ: 50.4, 83.8, 110.1, 112.6, 119.5, 120.0, 122.0, 126.3 (2C), 127.4, 128.7 (2C), 129.9, 137.1, 137.7. IR (thin film): 3061, 3000, 1495, 1448, 1455, 1348, 1331, 1307, 777, 744, 725 cm^{-1}. MS (EI): 333 (M^+, 100), 206 (43), 115 (7). Mass calcd for $C_{15}H_{12}NI$: 333.0015; found: 333.0012.

3.1.2. 2-Iodo-1-methoxymethylindole (28c). A solution of 2-iodoindole (1.21 g, 5.00 mmol) in THF (10 mL) was added dropwise to a slurry of NaH (300 mg, 7.50 mmol, washed with 3 mL of hexanes) in THF (5 mL) and DMF (2.5 mL) at 0°C. After stirring for 1 h, neat methoxymethyl bromide (0.55 mL, 6.06 mmol) was added dropwise to the reaction mixture. Upon disappearance of the starting material as indicated by TLC (1 h), the reaction mixture was diluted with Et_2O and washed with sat. NaCl. The organic layer was dried ($MgSO_4$) and the solvent was removed in vacuo. The crude material was purified by flash chromatography (90:10 hexane/EtOAc) to yield 1.29 g (90%) of 2-iodo-1-methoxymethylindole (**28c**), as a colorless oil.

^1H NMR (400 MHz, C_6D_6) δ: 2.91 (3H, s), 5.04 (2H, s), 6.75 (1H, d, *J*=0.6 Hz), 7.12–7.15 (2H, m), 7.33 (1H, m), 7.47 (1H, m). ^{13}C NMR (100 MHz, C_6D_6) δ: 55.1, 76.8, 82.7, 110.2, 114.0, 119.7, 120.8, 122.4, 130.4, 138.4. IR (thin film): 2934, 1458, 1441, 1393, 1339, 1304, 1281, 1225, 1190, 1161, 1125, 1098, 1078, 912, 783, 743, 590 cm^{-1}. MS (EI): 287 (M^+, 100), 256 (20), 205.1 (5), 130.1 (20), 129 (12), 115 (5). Mass calcd for $C_{10}H_{10}NIO$: 286.9807; found: 286.9811.

3.2. General procedure for the preparation of biindolyls (26)

3.2.1. 1-Methyl-2-(indol-2′-yl)indole (26a). *n*-BuLi (0.72 mL, 1.66 mmol, 2.3 M in hexane) was added to a solution of 2-iodo-1-methylindole (389 mg, 1.51 mmol) in THF (10 mL) at −78°C. After stirring 20 min, trimethyl borate (204 mg, 1.96 mmol) was added dropwise and the reaction mixture was warmed to 0°C and stirred 1.5 h. The solvent was removed in vacuo and 10 mL of toluene was added to the yellow oil. 2 M Na_2CO_3 (1.5 mL, purged with Ar) aqueous solution and powdered 2-iodoindole (300 mg, 1.24 mmol) in 3 mL of toluene were added to the reaction mixture. $Pd(PPh_3)_4$ was prepared by stirring PPh_3 (197 mg, 0.75 mmol) with $Pd(OAc)_2$ (34 mg, 0.15 mmol) in 3 mL of THF under Ar at rt for 15 min followed by the dropwise addition of *n*-BuLi (0.13 mL, 0.30 mmol). The catalyst reaction mixture was stirred for an additional 15 min at rt and the freshly made $Pd(PPh_3)_4$ was added to the reaction mixture. After refluxing for 18 h, the reaction mixture was cooled to rt and extracted into ether, washed with H_2O, dried ($MgSO_4$) and the solvent was removed in vacuo. Purification by flash chromatography (90:10 hexane/EtOAc) yielded 157 mg (51%) of 1-methyl-2-(indol-2′-yl)indole (**26a**) as a yellow solid.

^1H NMR (360 MHz, $CDCl_3$) δ: 3.95 (3H, s), 6.72 (1H, s), 6.75 (1H, s), 7.19 (2H, t, *J*=7.50 Hz), 7.25–7.33 (2H, m), 7.42 (2H, t, *J*=8.15 Hz), 7.69 (2H, t, *J*=8.16 Hz), 8.26 (1H, s (broad)). ^{13}C NMR (90 MHz, $CDCl_3$) δ: 31.3, 100.8, 102.4, 109.5, 110.8, 120.1, 120.3, 120.5, 120.6, 122.2, 122.7, 127.6, 128.8, 129.5, 133.0, 136.1, 138.5. IR ($CDCl_3$): 3411, 3010, 1470, 1451, 1428, 1391, 909, 802, 779, 735, 650 cm^{-1}. MS (EI): 247 (M^++1, 19), 246 (M^+, 100), 245 (30), 231 (6), 123 (8). Mass calcd for $C_{17}H_{14}N_2$: 246.1157; found: 246.1158.

3.2.2. 1-Benzyl-2-(indol-2′-yl)indole (26b). Following the general procedure for the synthesis of biindolyls, 1-benzyl-2-iodoindole (1.31 g, 3.95 mmol) was used to yield 790 mg (62%) of 1-benzyl-2-(indol-2′-yl)indole (**26b**) as a yellow solid after chromatography (90:10 hexane/EtOAc).

^1H NMR (360 MHz, $CDCl_3$) δ: 5.59 (2H, s), 6.54 (1H, s), 6.83 (1H, s), 7.11–7.13 (3H, m), 7.13–7.37 (8H, m), 7.58 (1H, d, *J*=7.87 Hz), 7.72 (1H, d, *J*=7.35 Hz), 8.21 (1H, s). ^{13}C NMR (90 MHz, $CDCl_3$) δ: 47.8, 101.7, 102.3, 110.2, 110.8, 120.3, 120.5, 120.7, 120.7, 122.6, 122.8, 125.9 (2C), 127.4, 128.0, 128.7, 129.0 (2C), 129.2, 133.2, 136.3, 138.0, 138.3. IR (thin film): 3410, 3100, 1495, 1452, 1437, 1394, 1338, 1323, 908, 783, 748, 727, 694 cm^{-1}. MS (EI): 322 (M^+, 100), 267 (21), 245 (16), 231 (60), 217 (17), 186 (16), 162 (42), 113 (24). Mass calcd for $C_{23}H_{18}N_2$: 322.1470; found: 322.1464.

3.2.3. 1-Methoxymethyl-2-(indol-2′-yl)indole (26c). Following the general procedure for the synthesis of biindolyls, 1-methoxymethyl-2-iodoindole (830 mg, 2.90 mmol) was used to yield 488 mg (61%) of 1-methoxymethyl-2-(indol-2′-yl) indole (**26c**) as a yellow solid after chromatography (85:15 hexane/EtOAc).

^1H NMR (400 MHz, C_6D_6) δ: 2.90 (3H, s), 4.99 (2H, s), 6.80 (1H, s), 7.08 (1H, s), 7.17–7.20 (1H, m), 7.23–7.30 (5H, m), 7.71 (1H, d, *J*=5.6 Hz), 7.80 (1H, d, *J*=8.1 Hz), 9.04 (1H, s (broad)). ^{13}C NMR (100 MHz, C_6D_6) δ: 55.4, 74.1, 103.3, 103.8, 109.4, 111.2, 120.5, 120.9, 120.9, 121.0, 122.6, 122.7, 128.6, 129.2, 129.6, 133.6, 137.1, 139.0. IR (KBr plate): 3412, 3373, 1460, 1441, 1387, 1348, 1331,

1314, 1292, 1159, 1101, 1071, 910, 793, 746, 727 cm^{-1}. MS (EI): 277.1 (M^++1, 26), 276.1 (M^+, 100), 245.1 (33), 244.1 (96), 243.1 (55), 231.1 (16), 204.1 (7). Mass calcd for $C_{18}H_{16}N_2O$: 276.1263; found: 276.1270.

3.3. General procedure for iodination and subsequent protection (33)

3.3.1. 3-Iodo-1-methyl-2-(1′-methylindol-2′-yl)indole (33a). 1-Methyl-2-(indol-2′-yl)indole (256 mg, 1.04 mmol) was dissolved in DMF (5 mL) and the solution cooled to 0°C. Powdered KOH (116 mg, 2.08 mmol) was added and the mixture stirred 5 min at 0°C. Iodine (289 mg, 1.14 mmol) in DMF (1 mL) was added dropwise resulting in a brown reaction mixture. After 5 min, the reaction mixture was diluted with Et_2O and washed with 15% $Na_2S_2O_3$. The organic layer was dried ($MgSO_4$) and the solvent was removed in vacuo to yield 3-iodo- 2-(1′-methylindol-2′-yl) indole, which was immediately carried forward to the next step.

NaH (60 mg, 1.5 mmol, washed with 2 mL of hexane) was suspended in DMF (3 mL) and brought to 0°C. Freshly prepared 3-iodo-2-(1′-methylindol-2′-yl)indole was dissolved in dry DMF (2 mL) and added dropwise to the NaH mixture. After 1 h at 0°C, MeI (213 mg, 1.5 mmol) was added dropwise to the green reaction mixture. After disappearance of the starting material as indicated by TLC, the reaction mixture was diluted with Et_2O and washed with H_2O. The organic layer was dried ($MgSO_4$) and the solvent was removed in vacuo. Purification by flash chromatography (75:25 hexane/EtOAc) yielded 387 mg (97%, two steps) of 3-iodo-1-methyl-2-(1′-methylindol-2′-yl)indole (**33a**) as a white solid.

^{1}H NMR (360 MHz, $CDCl_3$) δ: 3.65 (3H, s), 3.68 (3H, s), 6.74 (1H, s), 7.25 (1H, t, J=7.12 Hz), 7.30–7.48 (5H, m), 7.58 (1H, d, J=8.04 Hz), 7.76 (1H, d, J=7.88 Hz). ^{13}C NMR (90 MHz, $CDCl_3$) δ: 30.8, 31.6, 105.6, 109.8, 109.9, 110.1, 120.0, 120.8, 121.1, 121.5, 121.7, 122.4, 123.5, 123.7, 127.5, 129.9, 133.7, 137.7. IR ($CDCl_3$): 3154, 3061, 2942, 1611, 1462, 1325, 1233, 1101, 909, 735, 650 cm^{-1}. MS (EI): 386 (M^+, 100), 259 (67), 244 (21), 217 (7), 130 (12). Mass calcd for $C_{18}H_{15}N_2I$: 386.0280; found: 386.0278.

3.3.2. 1-Allyl-3-iodo-2-(1′-methylindol-2′-yl)indole (33b). Following the general procedure for iodination and subsequent protection, 1-methyl-2-(indol-2′-yl)indole (338 mg, 1.46 mmol) was used to yield 426 mg (75%, two steps) of 1-allyl-3-iodo-2-(1′-methylindol-2′-yl)indole (**33b**) as a white solid after chromatography (90:10 hexane/EtOAc).

^{1}H NMR (400 MHz, CD_2Cl_2) δ: 3.66 (3H, s), 4.63 (1H, ddt, J=16.9, 4.6, 1.8 Hz), 4.78 (1H, ddt, J=16.9, 5.3, 1.6 Hz), 4.83 (1H, dtd, J=17.1, 1.8, 1.3 Hz), 5.11 (1H, dtd, J=10.3, 1.6, 1.2 Hz), 5.84 (1H, dddd, J=17.1, 10.3, 5.3, 4.6 Hz), 6.71 (1H, d, J=0.8 Hz), 7.18–7.38 (5H, m), 7.45 (1H, dd, J=8.3, 0.8 Hz), 7.55 (1H, d, J=7.8 Hz), 7.71 (1H, d, J=7.9 Hz). ^{13}C NMR (100 MHz, CD_2Cl_2) δ: 30.9, 47.4, 63.8, 105.3, 109.9, 110.8, 116.5, 120.0, 120.9, 120.9, 121.4, 122.5, 123.5, 127.5, 130.0, 130.1, 133.2, 133.5, 137.1, 137.8. IR (KBr plate): 3056, 2936, 1456, 1424, 1383, 1352, 1338, 1310, 1209, 1013, 934, 799, 743 cm^{-1}. MS (EI): 412.0 (M^+, 100), 285.1 (55), 270.1 (24), 243.1 (43). Mass calcd for $C_{20}H_{17}IN_2$: 412.0437; Found: 412.0437.

3.3.3. 3-Iodo-1-benzenesulfonyl-2-(1′-benzylindol-2′-yl) indole (33c). Following the general procedure for iodination and subsequent protection, 1-benzyl-2-(indol-2′-yl)indole (283 mg, 0.88 mmol) was used to yield 330 mg (64%, two steps) of 3-iodo-1-benzenesulfonyl-2-(1′-benzylindol-2′-yl)indole (**33c**) as a white solid after chromatography (75:25 hexane/EtOAc).

^{1}H NMR (360 MHz, $CDCl_3$) δ: 5.53 (2H, s), 6.66 (1H, s), 7.11–7.21 (3H, m), 7.28–7.58 (12H, m), 7.70 (1H, d, J=7.66 Hz), 7.85 (1H, d, J=7.36 Hz), 8.45 (1H, d, J=8.38 Hz). ^{13}C NMR (90 MHz, $CDCl_3$) δ: 48.8, 80.9, 107.4, 110.8, 115.5, 119.9, 121.1, 122.7, 122.9, 124.7, 126.8, 126.9 (2C), 127.0 (2C), 127.1, 127.1, 128.3 (2C), 128.8 (2C), 129.3, 129.6, 132.1, 132.3, 134.1, 136.7, 137.2, 137.4. IR (thin film): 3080, 3000, 1458, 1446, 1377, 1346, 1316, 1190, 1174, 1089, 908, 750, 729, 684 cm^{-1}. MS (EI): 588 (M^+, 70), 448 (8), 397 (7), 320 (100), 243 (12). Mass calcd for $C_{29}H_{21}N_2SO_2I$: 588.0369; found: 588.0370.

3.3.4. 1-Allyl-3-iodo-2-(1′-benzylindol-2′-yl)indole (33d). Following the general procedure for iodination and subsequent protection, 1-benzyl-2-(indol-2′-yl)indole (332 mg, 1.03 mmol) was used to yield 339 mg (68%, two steps) of 1-allyl-3-iodo-2-(1′-benzylindol-2′-yl)indole (**33d**) as a white solid after chromatography (98:2 hexane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.31 (1H, dd, J=16.6, 4.7 Hz), 4.41 (1H, dd, J=16.6, 4.7 Hz), 4.99 (1H, dd, J=17.1, 1.0 Hz), 5.18 (1H, dd, J=10.3, 1.0 Hz), 5.32 (1H, d, J=16.1 Hz), 5.47 (1H, d, J=16.1 Hz), 5.78 (1H, ddt, J=17.1, 10.3, 4.7 Hz), 6.91 (1H, s), 6.92 (1H, d, J=8.2 Hz), 6.93 (1H, d, J=7.0 Hz), 7.20–7.26 (3H, m), 7.33–7.45 (5H, m), 7.53 (1H, d, J=8.2 Hz), 7.70 (1H, dd, J=7.0, 1.0 Hz), 7.86 (1H, d, J=7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 47.4, 48.4, 64.1, 107.0, 110.8, 111.0, 116.9, 120.4, 121.1, 121.4, 121.8, 123.0, 123.7, 127.1, 127.1, 127.5, 127.9, 128.6, 128.6, 129.7, 130.4, 133.3, 133.5, 137.1, 137.6, 137.7. IR (thin film): 3059, 1495, 1452, 1418, 1387, 1344, 1329, 1310, 1252, 1194, 1161, 1111, 1013, 908, 800, 739, 696 cm^{-1}. MS (FAB): 489 (M^++1, 100), 488 (M^+, 96), 361 (78). Mass calcd for $C_{26}H_{21}IN_2$: 488.07495; found: 488.0751.

3.3.5. 1-Allyl-3-iodo-2-(1′-methoxymethylindol-2′-yl) indole (33e). Following the general procedure for iodination and subsequent protection, 1-methoxymethyl-2-(indol-2′-yl)indole (772 mg, 2.80 mmol) was used to yield 885 mg (72%, two steps) of 1-allyl-3-iodo-2-(1′-methoxymethylindol-2′-yl)indole (**33e**) as a white solid after chromatography (90:10 hexane/EtOAc).

^{1}H NMR (400 MHz, C_6D_6) δ: 2.76 (3H, s), 4.20 (1H, dd, J=17.0, 4.9 Hz), 4.26 (1H, dd, J=17.0, 4.9 Hz), 4.64 (1H, d, J=17.9 Hz), 4.82 (1H, d, J=10.3 Hz), 5.08 (1H, d, J=10.8 Hz), 5.18 (1H, d, J=10.8 Hz), 5.46 (1H, ddt,

J=17.9, 10.3, 4.9 Hz), 6.74 (1H, s), 7.16 (1H, d, J=6.9 Hz), 7.24–7.30 (3H, m), 7.33 (1H, m), 7.56 (1H, d, J=8.1 Hz), 7.70 (1H, d, J=7.8 Hz), 7.78 (1H, dd, J=6.8, 1.8 Hz). ^{13}C NMR (100 MHz, C_6D_6) δ: 47.4, 55.6, 64.5, 75.3, 107.9, 111.0, 111.1, 116.2, 121.1, 121.3, 121.4, 121.9, 123.4, 123.7, 127.6, 128.3, 129.7, 130.6, 133.2, 137.4, 137.9. IR (KBr plate): 2942, 1456, 1437, 1381, 1368, 1346, 1305, 1285, 1013, 939, 908, 806, 741 cm^{-1}. MS (FAB): 442.1 (M^+, 100), 411.0 (26). Mass calcd for $C_{21}H_{19}IN_2O$: 442.0542; Found: 442.0531.

3.3.6. 1-*tert*-Butoxycarbonyl-2-iodo-3-(1′-methoxymethylindol-2′-yl)indole (33f). Following the general procedure for iodination and subsequent protection, 1-methoxymethyl-2-(indol-2′-yl)indole (232 mg, 0.84 mol) was used to yield 230 mg (53%) 1-*tert*-butoxycarbonyl-2-iodo-3-(1′-methoxymethylindol-2′-yl)indole (**33f**) as a yellow solid after chromatography (90:10 hexane/EtOAc).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.23 (9H, s), 3.21 (3H, s), 5.15 (1H, d, J=11.0 Hz), 5.47 (1H, d, J=11.0 Hz), 6.72 (1H, s), 7.24–7.60 (6H, m), 7.73 (1H, d, J=7.8 Hz), 8.32 (1H, d, J=8.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 27.5, 56.3, 75.5, 77.9, 84.1, 106.5, 110.1, 115.8, 120.4, 121.0, 122.2, 122.8, 123.7, 126.3, 127.9, 131.0, 131.3, 131.9, 136.6, 137.1, 148.2. IR (thin film): 3054, 2980, 2932, 1732, 1447, 1325, 1256, 1156, 1098, 1018, 916, 833, 754, 714 cm^{-1}. MS (EI): 502 (M^+, 100), 496 (20), 415 (37), 402 (55), 370 (99), 259 (40), 243 (70), 232 (53), 229 (28), 204 (17). Mass calcd for $C_{23}H_{23}IN_2O_3$: 502.0753; found: 502.0750.

3.4. General procedure for Fischer carbene synthesis (12)

3.4.1. [(1-Methyl-2-(1′-methylindol-2′-yl)indol-3-yl)methoxymethylene]pentacarbonylchromium (12a). *n*-BuLi (1.78 mL, 4.00 mmol, 2.25 M in hexane) was added dropwise to a solution of 3-iodo-1-methyl-2-(1′-methylindol-2′-yl)indole (1.286 g, 3.33 mmol) in a 50:50 mixture of THF:Et_2O (20 mL) at −78°C. After 1 h at −78°C, the reaction mixture was cannulated into a mixture of $Cr(CO)_6$ (733 mg, 3.33 mmol) in Et_2O (10 mL) at 0°C resulting in a red–orange reaction mixture. After 15 min, no solid was present in the reaction mixture and it was quenched with 0.25 mL of sat. aqueous Na_2CO_3 solution followed by MeOTf (1.09 g, 6.66 mmol), resulting in a bright red reaction mixture. When the reaction was complete, as evidenced by disappearance of the low R_f acylate on the TLC, the reaction mixture was diluted with CH_2Cl_2 and washed with sat. Na_2CO_3 solution. The organic layer was dried ($MgSO_4$) and plated onto diatomaceous earth. Flash chromatography (90:10 hexane/EtOAc) yielded 912 mg (55%) of [(1-methyl-2-(1′-methylindol-2′-yl)indol-3-yl)methoxymethylene]pentacarbonylchromium (**12a**) as a red solid.

^{1}H NMR (360 MHz, C_6D_6) δ: 2.72 (3H, s), 3.03 (3H, s), 3.62 (3H, s), 6.50 (1H, s), 6.89 (1H, d, J=7.74 Hz), 7.15–7.32 (5H, m), 7.69 (1H, d, J=7.82 Hz), 7.84 (1H, d, J=7.41 Hz). ^{13}C NMR (90 MHz, C_6D_6) δ: 30.2, 30.6, 65.2, 107.3, 109.9, 110.5, 120.9, 121.1, 121.5, 122.6, 123.0, 123.3, 123.9, 127.1, 127.2, 129.1, 134.8, 137.3, 138.8, 216.7, 224.7, (carbene carbon not observed). IR (thin film): 3100, 3010, 2058, 1930, 1849, 1462, 1387, 1329, 1217, 839, 748 cm^{-1}. MS (FAB): 494 (M^+, 20), 466 (25), 440 (20), 410 (45), 382 (43). Mass calcd for $C_{25}H_{18}N_2O_6Cr$: 494.0570; found: 494.0575.

3.4.2. [(1-Allyl-2-(1′-methylindol-2′-yl)indol-3-yl)methoxymethylene]pentacarbonylchromium (12b). Following the general procedure for Fischer carbene preparation,1-allyl-3-iodo-2-(1′-methylindol-2′-yl)indole (158 mg, 0.38 mmol) was used to yield 128 mg (66%) of [(1-allyl-2-(1′-methylindol-2′-yl)indol-3-yl)methoxymethylene]pentacarbonylchromium (**12b**) as a red solid together with a fluorescent impurity after chromatography (80:20 hexane/EtOAc). Chromium carbene **12b** was the major product as evidenced by ^{1}H and ^{13}C NMR.

^{1}H NMR (200 MHz, C_6D_6) δ: 3.06 (3H, s), 3.71 (3H, s), 3.94–3.98 (2H, m), 4.54 (1H, d, J=16.1 Hz), 4.77 (1H, d, J=10.2 Hz), 5.29–5.43 (1H, m), 6.69 (1H, s), 7.00–7.28 (6H, m), 7.67 (1H, d, J=7.1 Hz), 7.86 (1H, d, J=6.3 Hz). ^{13}C NMR (100 MHz, acetone-d_6) δ: 33.1, 46.4, 66.6, 106.6, 110.0, 111.6, 116.1, 120.0, 120.4, 120.9, 122.3, 122.7, 123.8, 127.6, 128.6, 129.3, 131.6, 133.1, 134.4, 136.5, 138.8, 216.0, 224.9, 343.5.

3.4.3. [(1-Allyl-2-(1′-methoxymethylindol-2′-yl)indol-3-yl) methoxymethylene]-pentacarbonylchromium (12e). Following the general procedure for Fischer carbene preparation, 1-allyl-3-iodo-2-(1′-methoxymethylindol-2′-yl)indole (221 mg, 0.50 mmol) was used to yield 157 mg (59%) of [(1-allyl-2-(1′-methoxymethylindol-2′-yl)indol-3-yl) methoxymethylene]pentacarbonylchromium (**12e**) as a red solid, together with a fluorescent impurity after chromatography (85:15 hexane/EtOAc).

^{1}H NMR (200 Hz, $CDCl_3$) δ: 3.23 (3H, s), 4.45 (3H, s), 4.58–4.65 (2H, m), 4.80–4.95 (2H, m), 5.17 (1H, d, J=9.9 Hz), 5.24 (1H, d, J=9.9 Hz), 5.82–5.84 (1H, m), 6.86 (1H, s), 7.25–7.35 (6H, m), 7.50 (1H, d, J=7.8 Hz), 7.71 (1H, d, J=8.3 Hz). ^{13}C NMR (100 Hz, acetone-d_6) δ: 46.4, 55.6, 66.9, 74.6, 106.3, 108.4, 110.3, 111.4, 116.4, 120.5, 121.0, 121.9, 122.3, 123.3, 123.7, 127.7, 127.8, 129.1, 133.5, 136.1, 138.9, 216.2, 225.0, (carbene carbon not observed).

3.4.4. [(1-*tert*-Butoxycarbonyl-2-(1′-methoxymethylindol-2'-yl)indol-3-yl)methoxymethylene]-pentacarbonylchromium (12f). Following the general procedure for Fischer carbene preparation, 1-*tert*-butoxycarbonyl-2-iodo-3-(1′-methoxymethylindol-2′-yl)indole (0.170 g, 0.339 mmol) was used to yield 85 mg (42%) of [(1-*tert*-butoxycarbonyl-2-(1′-methoxymethylindol-2′-yl)indol-3-yl)-methoxymethylene]pentacarbonylchromium (**12f**) as a red solid after chromatography (95:5 hexane/EtOAc).

Note: Due to restricted rotation about more than one bond, the NMR spectra were unusually complex due to the presence of several rotomers. ^{1}H NMR (500 Hz, $CDCl_3$) δ: 1.16 (9H, s), 1.21 (9H, s), 1.25 (9H, s), 3.13 (3H, s), 3.21 (3H, s), 3.39 (3H, s), 3.61 (3H, s), 3.70 (3H, s), 5.19–5.41 (2H, m), 6.57 (1H, s), 7.16–7.68 (6H, m), 8.20–8.37 (2H, m). ^{13}C NMR (125 Hz, acetone-d_6) δ: 22.5, 27.3, 27.4, 28.0, 28.1, 31.5, 34.6, 51.4, 62.2, 75.2, 75.7, 79.7, 84.5, 84.9, 105.4, 107.2, 109.7, 110.0, 110.7,

115.2, 115.9, 119.6, 120.3, 120.5, 120.6, 120.8, 120.9, 121.3, 121.9, 122.1, 122.5, 122.6, 123.2, 123.4, 123.9, 124.0, 124.1, 125.7, 126.0, 126.8, 127.89, 128.0, 129.8, 132.4, 134.2, 136.3, 136.9, 137.4, 137.6, 149.0, 149.5, 163.3, 164.2, 215.3, 224.2, 351.6. IR(thin film): 3056, 2976, 2930, 2062, 1935, 1738, 1698, 1451, 1346, 1254, 1148, 1082, 1017, 916, 841, 748, 646 cm^{-1}. MS (FAB): 610.2 (M^+, 4), 526.1 (47), 470.1 (77), 418.1 (51). Mass calcd for $C_{27}H_{26}N_2O_6Cr$ (loss of 3 COs): 526.1207; found: 526.1196.

3.5. General procedure for benzannulation via photolysis (13)

3.5.1. 6-Hydroxyl-5-methoxy-11,12-dimethyl-11,12-dihydroindolo[2,3-*a*]carbazole (13a). [(1-Methyl-2-(1′-methylindol-2′-yl)indol-3-yl)methoxymethylene]pentacarbonylchromium (38 mg, 0.077 mmol) was dissolved in toluene (3 mL) and placed in a pyrex pressure tube. The pressure tube was purged with Ar by evacuating it and then filling it with Ar (2×). The pressure tube was then evacuated and filled with 20 psi of CO (2×). Photolysis proceeded using a medium pressure mercury lamp, UV 450W immersion type from Ace Glass, which was surrounded by a quartz cooling tube. After 3 h, the reaction was complete as evidenced by disappearance of the bright-red color of the carbene. The crude product was plated onto diatomaceous earth and was purified by flash chromatography (75:25 hexane/EtOAc) to yield 13 mg (51%) of 6-hydroxyl-5-methoxy-11,12-dimethyl-11,12-dihydroindolo[2,3-*a*]carbazole (**13a**) as a white solid.

^{1}H NMR (360 MHz, DMSO-d_6) δ: 3.93 (3H, s), 4.14 (3H, s), 4.16 (3H, s), 7.21–7.27 (2H, m), 7.42–7.48 (2H, m), 7.59–7.63 (2H, m), 8.22 (1H, d, J=7.74 Hz), 8.37 (1H, d, J=7.68 Hz), 9.37 (1H, s). ^{13}C NMR (90 MHz, DMSO-d_6) δ: 36.5, 36.8, 60.9, 110.3, 110.8, 113.8, 116.8, 119.8, 119.9, 121.97, 122.6, 122.7, 123.3, 124.0, 125.0, 125.4, 126.3, 135.2, 139.1, 143.0, 143.5. IR (KBr): 3500–3100 (br), 3050, 3020, 2980, 2940, 1600, 1504, 1458, 1421, 1363, 1321, 1261, 1155, 1095, 989, 922, 790, 741, 640 cm^{-1}. MS (EI): 330.1 (M^+, 85), 315.1 (100), 287.1 (6), 244.1 (5), 165.1 (7), 143.6 (6). Mass calcd for $C_{21}H_{18}N_2O_2$: 330.1368; found: 330.1371.

3.5.2. 12-Allyl-6-hydroxy-5-methoxy-11-methyl-11,12-dihydroindolo-[2,3-*a*]carbazole (13b). Following the general procedure for benzannulation via photolysis, [(1-allyl-2-(1′-methylindol-2′-yl)indol-3-yl)methoxymethylene]-pentacarbonylchromium (86.6 mg, 0.170 mmol, impure,) was used to yield 35.2 mg (58%) of 12-allyl-6-hydroxy-5-methoxy-11-methyl-11,12-dihydroindolo-[2,3-*a*]carbazole (**13b**) as a yellow solid after chromatography (85:15 hexane/EtOAc).

^{1}H NMR (360 MHz, $CDCl_3$) δ: 4.03 (3H, s), 4.12 (3H, s), 4.99 (2H, m), 5.44 (1H, dd, J=10.6, 1.3 Hz), 5.49 (1H, dd, J=17.2, 1.3 Hz), 6.15 (1H, s), 6.20 (1H, ddt, J=17.2, 10.6, 3.8 Hz), 7.33–7.38 (2H, m), 7.42 (1H, d, J=8.0 Hz), 7.48–7.7.52 (3H, m), 8.33 (1H, d, J=7.8 Hz), 8.50 (1H, d, J=7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 34.8, 50.3, 60.1, 108.4, 110.2, 111.8, 115.7, 116.1, 118.9, 119.3, 120.9, 121.6, 122.5, 122.8, 122.9, 123.8, 124.1, 125.9, 132.8, 133.2, 137.4, 142.5, 143.0. IR (thin film): 3532, 3393, 3054, 2930, 2855, 1499, 1468, 1454, 1239, 1429, 1344, 1321, 1248, 1146, 908, 735 cm^{-1}. MS (EI): 356.2 (M^+, 100), 341.1 (25), 315.1 (78), 300.1 (58), 271.1 (22), 244.1 (22). Mass calcd for $C_{23}H_{20}N_2O_2$: 356.1525; found: 356.1532.

3.5.3. 12-Allyl-6-hydroxy-5-methoxy-11-methoxymethyl-11,12-dihydroindolo[2,3-*a*]carbazole (13e). Following the general procedure for benzannulation via photolysis, [(1-allyl-2-(1′-methoxymethyl-indol-2′-yl)indol-3-yl)methoxy methylene]pentacarbonylchromium (82 mg, 0.152 mmol, impure) was used to yield 59.6 mg (63%) of 12-allyl-6-hydroxy-5-methoxy-11-methoxymethyl-11,12-dihydroindolo-[2,3-*a*]carbazole (**13e**) as a pale yellow solid after chromatography (80:20 hexane/EtOAc).

^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.38 (3H, s), 3.96 (3H, s), 5.13 (2H, s (broad)), 5.16 (1H, d, J=16.4 Hz), 5.25 (1H, d, J=10.3 Hz), 5.63 (2H, s (broad)), 6.01 (1H, s), 6.12 (1H, m), 7.24–7.31 (2H, m), 7.39–7.7.47 (3H, m), 7.62 (1H, d, J=7.8 Hz), 8.26 (1H, d, J=7.6 Hz), 8.42 (1H, d, J=7.6 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 48.4, 55.4, 60.4, 77.4, 110.7, 111.2, 114.2, 116.1, 117.4, 120.0, 120.6, 121.7, 122.4, 122.6, 122.9, 124.4, 124.5, 125.0, 125.2, 134.7, 135.8, 139.0, 142.3, 143.2. IR (KBr plate): 3409, 3056, 2994, 2926, 1499, 1453, 1431, 1391, 1323, 1250, 1215, 1180, 1144, 1103, 1061, 1026, 1001, 988, 945, 928, 743 cm^{-1}. MS (EI): 386.2 (M^+, 100), 341.1 (28), 326.1 (16), 311.1 (19). Mass calcd for $C_{24}H_{22}N_2O_3$: 386.1630; found: 386.1637.

3.5.4. 12-*tert*-Butoxycarbonyl-6-hydroxy-5-methoxy-11-methoxymethyl-11,12-dihydroindolo [2,3-*a*]carbazole (13f). Following the general procedure for benzannulation via photolysis, [(1-*tert*-butoxycarbonyl-2-(1′-methoxymethyl-indol-2′-yl)indol-3-yl)methoxymethylene]pentacarbonyl-chromium (0.042 g, 0.0702 mmol) was used to yield 22 mg (71%) of 12-*tert*-butoxycarbonyl-6-hydroxy-5-methoxy-11-methoxymethyl-11,12-dihydroindolo[2,3-*a*]carbazole (**13f**) as a yellow oil after chromatography (90:10 hexane/EtOAc).

^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.62 (9H, s), 2.68 (3H, s), 3.94 (3H, s), 5.75 (2H, s), 7.25–7.32 (1H, m), 7.42–7.55 (3H, m), 7.75 (1H, d, J=8.09 Hz), 8.10 (1H, d,J=8.24 Hz), 8.21 (1H, d, J=7.69 Hz), 8.34 (1H, d, J=7.61 Hz), 9.91 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 25.4, 27.9, 56.0, 61.1, 84.7, 111.5, 115.2, 116.3, 118.2, 120.0, 120.8, 122.2, 122.8, 124.4, 125.6, 126.1, 127.0, 128.5, 129.2, 135.7, 140.1, 141.9, 142.9, 152.0. IR (thin film): 3357, 2926, 1732, 1651, 1504, 1454, 1372, 1260, 1150, 1022, 909, 750 cm^{-1}. MS (FAB): 446.2 (M^+, 86), 415.2 (19), 359.0 (100), 345.1 (48). Mass calcd for $C_{26}H_{26}N_2O_5$: 446.1835; found: 446.1841.

3.6. General procedure for thermal benzannulation (14)

3.6.1. 6-*tert*-Butylamino-5-methoxy-11,12-dimethyl-11,12-dihydroindolo[2,3-*a*]carbazole (14a). *t*-Butyl isonitrile (0.021 mL, 0.186 mmol) was added to a solution of [(1-methyl-2-(1′-methylindol-2′-yl)indol-3-yl)methoxymethylene]pentacarbonylchromium (46 mg, 0.093 mmol) in toluene (3 mL) at 0°C. After 1 h at 0°C, the carbene was

completely reacted as evidenced by TLC. The reaction mixture was then refluxed 5 h. The crude reaction mixture was then plated onto diatomaceous earth and purified by flash chromatography (90:10 hexane/EtOAc) yielding 32 mg (89%) of 6-*tert*-butylamino-5-methoxy-11,12-dimethyl-11,12-dihydroindolo[2,3-*a*]carbazole (**14a**) as a yellow solid.

^{1}H NMR (360 MHz, $CDCl_3$) δ: 1.32 (9H, s), 4.01 (3H, s), 4.13 (3H, s), 4.16 (3H, s), 7.26–7.36 (3H, m), 7.46–7.54 (4H, m), 8.35 (1H, d, J=7.80 Hz), 8.77 (1H, d, J=7.87 Hz). ^{13}C NMR (90 MHz, $CDCl_3$) δ: 29.9 (3C), 30.7, 36.3, 36.5, 60.5, 109.7, 109.8 (2C), 116.8, 119.2, 120.1, 122.3 (2C), 123.1 (2C), 123.3, 124.7, 124.9 (2C), 126.9, 143.9, 144.2, 145.5. IR (thin film): 2960 (broad), 1453, 1318, 1153, 1091, 744 cm^{-1}. MS: 385.2 (M^+, 100), 370.2 (8), 328.1 (62), 314.1 (70), 300.1 (20), 384.1 (17), 270.1 (7). Mass calcd for $C_{25}H_{27}N_3O$: 385.2151; found: 385.2150.

3.6.2. 12-Allyl-6-*tert*-butylamino-5-methoxy-11-methyl-11,12-dihydro-indolo[2,3-*a*]carbazole (14b). Following the general procedure for thermal benzannulation, [(1-allyl-2-(1′-methylindol-2′-yl)indol-3-yl)methoxymethylene] pentacarbonylchromium (128 mg, 0.246 mmol, impure) was used to yield 60 mg (58%) of 12-allyl-6-*tert*-butylamino-5-methoxy-11-methyl-11,12-dihydro-indolo[2,3-*a*]-carbazole (**14b**) as a white solid after chromatography (90:10 hexane/EtOAc).

^{1}H NMR (400 MHz, C_6D_6) δ: 1.50 (9H, s), 3.44 (3H, s), 3.52 (1H, s (broad)), 3.85 (3H, s), 4.44 (2H, m), 5.12 (1H, dd, J=10.6, 1.4 Hz), 5.27 (1H, dd, J=17.3, 1.4 Hz), 5.70 (1H, ddt, J=17.3, 10.6, 4.5 Hz), 7.28 (1H, d, J=8.1 Hz), 7.43–7.56 (5H, m), 8.69 (1H, d, J=7.6 Hz), 9.26 (1H, d, J=7.8 Hz). ^{13}C NMR (100 MHz, CD_2Cl_2) δ: 29.9, 36.1, 51.6, 56.4, 60.4, 110.0, 111.3, 117.0, 117.4, 119.1, 120.5, 122.3, 122.5, 123.2, 124.1, 124.8, 125.0, 125.5, 127.0, 127.3, 127.3, 134.1, 144.1, 144.3, 145.7. IR (KBr plate): 3081, 3059, 2977, 1474, 1451, 1418, 1364, 1323, 1273, 1223, 1148, 1098, 1009, 999, 932, 823, 747 cm^{-1}. MS (FAB): 411.2 (M^+, 100), 370.2 (11), 354.2 (51), 340.1 (25), 314.1 (82), 299.1 (29), 284.1 (27), 270.1 (15). Mass calcd for $C_{27}H_{29}N_3O$: 411.2304; found: 411.2311.

3.6.3. 12-Allyl-5-*tert*-butylamino-6-methoxy-11-methoxymethyl-11,12-dihydroindolo[2,3-*a*]carbazole (14e). Following the general procedure for thermal benzannulation, [(1-allyl-2-(1′-methoxymethylindol-2′-yl)indol-3-yl)methoxymethylene]pentacarbonylchromium (55 mg, 0.1 mmol, impure) was used to yield 33 mg (74%) of 12-allyl-5-*tert*-butylamino-6-methoxy-11-methoxymethyl-11,12-dihydroindolo[2,3-*a*]-carbazole (**14e**) as a white solid after chromatography (90:10 hexane/EtOAc).

^{1}H NMR (400 MHz, C_6D_6) δ: 1.47 (9H, s), 3.04 (3H, s), 3.50 (1H, s (broad)), 3.83 (3H, s), 4.84 (2H, m), 5.12 (1H, dd, J=10.6, 1.4 Hz), 5.22 (2H, s), 5.31 (1H, dd, J=17.3, 1.4 Hz), 5.86 (1H, ddt, J=17.3, 10.6, 3.7 Hz), 7.44–7.51 (5H, m), 7.56 (1H, d, J=7.3 Hz), 8.67 (1H, d, J=7.6 Hz), 9.30 (1H, dd, J=7.1, 2.0 Hz). ^{13}C NMR (100 MHz, CD_2Cl_2) δ: 32.0, 52.0, 57.9, 58.6, 62.7, 80.8, 112.7, 113.4, 118.4, 119.8, 122.4, 122.6, 124.4, 125.2, 125.6, 125.9, 127.2, 127.3, 127.4, 128.4, 129.3, 129.4, 136.6, 145.9, 146.0, 148.7. IR (KBr plate): 3600–3200 (broad), 2963, 1491, 1449, 1420, 1389, 1364, 1342, 1325, 1271, 1198, 1146, 1105, 1074, 1005, 745 cm^{-1}. MS (FAB): 441.2 (M^+, 100), 384 (11). Mass calcd for $C_{28}H_{31}N_3O_2$: 441.2416; found: 441.2417.

3.6.4. 12-*tert*-Butoxycarbonyl-6-*tert*-butylamino-5-methoxy-11-methoxymethyl-11,12-dihydroindole[2,3-*a*]carbazole (14f). Following the general procedure for thermal benzannulation, [(1-*tert*-butoxycarbonyl-2-(1′-methoxymethylindol-2′-yl)indol-3-yl)methoxymethylene]pentacarbonylchromium (0.042 g, 0.070 mmol) was used to yield 24 mg (68%) of 12-*tert*-butoxycarbonyl-6-*tert*-butylamino-5-methoxy-11-methoxymethyl-11,12-dihydroindole[2,3-*a*] carbazole (**14f**) as a white solid after chromatography (95:5 hexane/EtOAc).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.38 (9H, s), 1.74 (9H, s), 2.72 (3H, s), 3.50 (1H, s (broad)), 4.02 (3H, s), 5.83 (2H, s), 7.42–7.53 (4H, m), 7.62 (1H, d, J=8.1 Hz), 8.19 (1H, d, J=8.0 Hz), 8.35 (1H, d, J=7.5 Hz), 8.71 (1H, d, J=7.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 28.1, 30.0, 30.7, 55.8, 56.6, 60.2, 84.2, 111.3, 116.2, 119.8, 120.2, 122.2, 122.4, 122.9, 123.4, 123.8, 125.0, 125.6, 126.0, 126.6, 128.7, 131.5, 140.2, 141.7, 145.2, 151.9. IR (thin film): 3054, 2978, 2824, 1728, 1450, 1369, 1294, 1246, 1152, 1084, 910, 733, 655 cm^{-1}. MS (FAB): 501.2 (M^+, 95), 414.1 (55), 356.1 (84), 329.9 (100). Mass calcd for $C_{30}H_{35}N_3O_4$: 501.2633; found: 501.2628.

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