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MultifoldC-C Coupling and Unorthodox Cyclization Catalysisfor Selective Synthesis of Indolo-triarylmethanes, Indolocarbazoles and Analogues: A Control Experiment Study

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ABSTRACT: The selective construction of medicinally and synthetically important indole-based unsymmetrical triarylmethanes using indoles and aldehydes is challenging because the significant nucleophilicity of indole leads to C-C coupling with an azafulven intermediate to built up the alternative product bis(indolyl)methanes, which may be useful synthons. A new straightforward ligand-free Cu^{II}-catalytic strategy for easy syntheses of unsymmetrical indolo-triarylmethanes and new bisindolylbenzoyl analogues is established through the dual C-C coupling of an assembly of three reaction partners comprising aldehydes, indoles and arylboronic acids. More importantly, this approach is exploited for multifold C-C coupling cyclization reaction with C-C cleavage using sym-

metrical bisindolylbenzoylmethanes in the presence of an organic base and aerial molecular oxygen as a stoichiometric oxidant. In contrast to formation of a simple cyclocondensation product indolocarbazole, it undergoes unprecedented selective pseudo fourcomponent tandem oxidative cyclization with fragmentation from an 1,3-dicarbonyl compounds to produce valuable fused-5,7dihydroindolo[2,3-*b*]carbazoles through the functionalization of indole-sp²C₂-H and sp³C-H of active methylene residue. For better understanding of the new reactions, we have studied various competition experiments, ESI-MS and 3D Mid-IR-ATR spectral analyses of the ongoing reactions. The predicted DFT-transition state model is also in agreement with the experimental results.

KEYWORDS: Diverse catalysis, multifold C-C coupled cyclization, high selectivity, indolo-triarylmethanes, indolo[2,3-b]carbazoles

INTRODUCTION

C-C bond formation is a fundamental reaction, and multifold C-C coupling catalysis¹ has recently attracted considerable attention as a convenient way to frame desirable molecular complexity for the design of an appropriate assembly of simple precursors.² The selective construction of valuable unsymmetrical indole-based triarylmethanes³ (4, *path a*, Scheme 1) using indoles (1) and aldehydes (2) is challenging because the significant nucleophilicity of indole leads to the formation of the alternative product *bis*(indolyl)methane (5, *path b*) through C-C coupling with an azafulven intermediate (II). In most reports, two of the three aryl groups are the same, imposing an obstacle to the fine-tuning of the chemical, medicinal and material properties of the resulting

triarylmethanes. On the other hand, arylboronic acids⁴ are used in organic extensively chemistry as chemical building blocks because of their commercial availability, low toxicity and wide tolerance. One of the important chemical reactivities of boronic acids is the trans-metallation of its organic residue with an appropriate transition metal.⁵ Thus, it would be beneficial if we use arylboronic acid (3) as the third reaction partner during indole (1)-aldehyde (2) coupling through the development of an efficient catalyst for the selective dual C-C coupling process (path a) to achieve unsymmetrical triarylmethanes (4). The properly designed and synthesized other possible product, bisindolylmethane (path b, 5) analogoues, would be useful synthons if both the sp²C₂-H groups undergo cyclization with release of the sp³C-*H*, leading to the highly selective construction of ubiquitous carbazole⁶ and



indolocarbazole⁷ core structures. Thus, the transformation of two competing pathways (4 and 5; *path a/path b*) for the selective building up of complex frameworks through a suitable catalysis strategy will be useful in modern organic synthesis.

Scheme 1. Two Possible Catalytic Pathways to Triarylmethanes



Indole is a key building block in a wide range of valuable natural products, pharmaceuticals, agrochemicals and materials,⁸⁻¹⁰ which prompted us to develop a mild catalysis approach to achieve simple and complex indole architectures. Indole-based triarvlmethanes constitute an important class of compounds because of their omnipresence in reductase inhibitors, antiviral agents, anticancer drug, dye materials, bioactive alkaloids and other natural products.9 The indole-based compounds were developed as an anti-breast cancer active nonsteroidal aromatase inhibitor (A, Fig. 1),^{10a} antibiotic and anticancer trisindoline alkaloid (\mathbf{B}) ,^{10b} the antitumor drug rebecamycin (\mathbf{C}) ,^{10c} the highperformance OFET material indolo[3,2-b]carbazoles (ICZ, D)^{10d} and multi cancer cell line active natural product glycosmisine B (E).^{10e} The syntheses of symmetrical bis-indolo-triarylmethanes were investigated via the Friedel-Crafts addition of electron-rich arenes to aldehydes and imines.¹¹ However, the direct synthesis of unsymmetrical indole-based triarylmethanes has been less explored, and recent reports have involved InCl₃-, FeCl₃-, (EtCp)₂ZrCl₂-C₈F₁₇SO₃Ag-, ZnCl₂- and PdCl₂-catalyzed reactions.¹² The syntheses of common unsymmetrical triarylmethanes have been studied thoroughly.¹³ However, the methods have limitations in terms of utilizing expensive metallic compounds, two catalysts, stoichiometric oxidants, ligands, hazardous and specially designed substrates, stringent reaction conditions and multistep reactions, as well as the formation of symmetrical analogues. Moreover, mechanistic pathway for the synthesis of unsymmetrical indole-based triarylmethanes is not studied thoroughly.

Indolocarbazole was first isolated in 1977 and showed important biological activities and pharmaceutical applications (Figure 1).¹⁴ Rigid coplanar structural features with the strong π -electron density of 5,11-dihydroindolo[3,2-*b*]carbazole have led to electronrich π -conjugated backbones for innovative materials displaying properties useful for photophysical, electronic, optoelectronic, OFET and other organic electronic applications of extreme sensitivity.^{10b-d,15} In contrast to the diverse applications of indolo[2,3*b*]carbazole and isomeric indole-bearing carbazoles, their general

synthesis remains unexplored due to the constructional strains. The typical indole-aldehyde condensation widely used for the synthesis of indolo[3,2-b]carbazoles failed to provide the isomeric indolo[2,3-b]carbazoles; however, a few methods have been reported, such as oxidative indole-arylaldehyde condensation with POCl₃ and acids, the intramolecular cyclization of specially designed ironcarbonyl-activated aromatic diamine precursors, the double-intramolecular Buchwald-Hartwig reaction and Pd(II)-Cu(II) catalyzed carbazoles-indole cyclization.¹⁶ Interestingly, the carbazoles-bearing indole moiety also displayed important medicinal^{10e} and solar cell applications.¹⁷ Thus, it will be beneficial to develop an efficient general strategy for the diverse syntheses of valuable indole-based functionalized unsymmetrical triarylmethanes, diindolylbenzoyl analogues, indole substituted carbazole and indolo[3,2-b]carbazoles, which possess innovative medicinal and organic electronic properties.



Figure 1. Valuable indole-based natural and synthetic compounds

RESULTS AND DISCUSSION

At the outset, we studied the dual C-C coupling process using indole (1a), 4-methylbenzaldehyde (2a), and phenylboronic acid (3a) as three reacting partners to survey the reaction parameters, and the results are summarized in Table 1. The reaction was first performed at ambient temperature (not shown) and subsequently heated at 100 °C for 12-18 h with potential catalysts such as rare earth (entries 1-3) and transition metal compounds (entries 4-7). The desired product 4a or byproduct 5a was not detected in the post reaction mixtures. To our delight, with the use of Cu(OTf)₂ as a catalyst (entry 8), 4a was obtained in 65% yield. Both the vield (79%) and catalyst loading (5mol%) were greatly improved on performing the reaction at 80 °C (entry 9). The reaction did not occur at room temperature (entry 10), and the yield was reduced if the reaction temperature was reduced even slightly to 70 °C (entry 11). Similar observations were made upon conducting the reaction under argon atmosphere (entry 12). The results of changing the aprotic polar to nonpolar solvents (entries 13-17) or using various Cu^{II} and Cu^I-compounds (entries 18-22), different ligands (23,24), bases (entries 25,26) and combo-catalysts (entry 27) were not encouraging.

Next, we have studied the general applicability of the developed reaction conditions (entry 9, Table 1) using various substituted aldehydes (1), indoles (2) and arylboronic acids (3) to achieve functionalized indole-based unsymmetrical triarylmethanes (4, Scheme 2), though we were not totally successful in eliminating the bisindolyl byproduct 5 (<5%). Both aliphatic and aromatic aldehydes were tried and were transformed into the corresponding desired products (4a-r) under the reaction conditions. Aldehydes substituted with both electron withdrawing (4c,e-j,l) and electron donating groups (4a,b,d,o,r) were able to respond to the reaction. Among the synthesized indole derivatives, the reaction went very well when sterically hindered aldehydes (4b,e,g,h,k,n-p) were Table 1. Survey of dual C-C coupling reaction to triarylmethane (4a)^a

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^aReaction: **1a** (1.2mmol), **2a** (1 mmol) and **3a** (1.2mmol); ^bCatalyst loading: 10 mol%; ^cVolume of solvent: 3 mL; ^dYield of pure **4a** and **5a** after silica-gel column chromatography; ^e5 mol%; ^f10 mol%; ^g1 mmol.

used. Even 5-methoxy, 5-bromo, 5-nitro and 2-methylindole, N-methyl indole derivatives (**4f,h-j,r**) yielded corresponding triarylmethanes. In the case of arylboronic acids, other than phenylboronic acid, a 2-methyl analogue is also capable of yielding the desired product (**4g**), allowing the installation of a great diversity of substituents on the triarylmethane template.

To obtain a close look into the probable reaction pathway of the three-component reaction, we have performed some control experiments (Scheme 3). We started the reaction using the possible intermediate phenyl(*p*-tolyl)methanol (**6a**) and reactant indole (**1a**, **Scheme 2**. Selective Synthesis of Indolo-triarylmethanes (**4**)



eq. i, Scheme 3) as well as the alternative intermediate (1H-indol-3-yl)(p-tolyl)methanol (6b) and substrate phenylboronic acid (3a, eq. ii) in a 1:1 ratio under similar reaction conditions (entry 9, Table 1). Both reactions were quenched in 1h, and the desired product 4a was obtained for both reactions, though the yields were distinctly different. A much better yield (88%)was found for the first reaction between indole (1a) and phenyl(*p*-tolyl)methanol (6a). A relatively low yield (4a, 67%) was afforded (eq. ii) from coupling between (1H-indol-3-yl)(p-tolyl)methanol (6b) and phenylboronic acid (3a). Interestingly, if we added ntolylbenzaldehyde (2a) and phenylboronic acid (3a) under similar reaction conditions, phenyl(p-tolyl)methanol (6a) was not generated even after 12 h (eq. iii). From these control experiments, it is concluded that the reaction passes through the formation of the intermediate (1H-indol-3-yl)(p-tolyl)methanol (I), which was also detected in the mass spectra of the reaction mixture (vide infra, intermediate I-1 in Scheme 4).

A reasonable mechanism for the formation of the indolotriarylmethane product is proposed in Scheme 4and was corroborated by the mass study data on the reaction mixture containing the reaction partner 4-nitrobenzaldehyde, phenylboronic acid and indole. The two proposed intermediates **I-1** and **I-2** were detected by ESI-MS analyses (Supporting Information). We also attempted a theoretical DFT study for the Cu(OTf)₂-catalyzed synthesis of triarylmethane. All calculations were performed using the Gaussian 09 package of programs. The structures were optimized using the DFT method B3LYP with basis set SDD. Vibration analyses were **Scheme 3.** Control Experiment Study



performed to check stable geometries with no imaginary frequencies. The transition state was determined using the QST3approach. For the located transition structure, only one imaginary frequency was found. Intrinsic reaction coordinate (IRC) calculation was performed to connect the transition structure unambiguously with the reactants. The energy profile diagram of the final step (Scheme 4) of the reaction is displayed in Fig. 2 along with the DFT-optimized structures of the intermediate (I-2), transition state (TS) and final product. The transition state energy barrier is 0.0015kcal/mol. Thus, the prediction is in agreement with the experimental data on the rapid dual C-C coupling reaction.

Scheme 4. Plausible Mechanistic Pathway to Indolotriarylmethane





Figure 2. Important transition state and expected intermediate as predicted by DFT calculation (Gaussian 09). DFT-optimized structures are in violet box.

We have also monitored the progress of the catalytic process using 3D Mid-IR-ATR spectral analyses of the ongoing reaction among 4-nitrobenzaldehyde, phenylboronic acid and indole. As a reference compound, we found two symbolic peaks for 4nitrobenzaldehyde (1712 cm⁻¹ and 1536 cm⁻¹; red line, Fig. 3) and one distinct peak at 1604 cm⁻¹ for phenyl boronic acid (deep green, Fig. 3). As expected, the peaks at 1712 cm^{-1} and 1536 cm^{-1} for aldehyde vanished entirely within 30 min after the commencement of the reaction (Fig. 4). However, there was no prominent change in the characteristic peaks for indole in the 3D surface, since the product itself bears the indole residue. After 30 minutes, the peak attributable to phenylboronic acid at 1604 cm⁻¹ started decreasing (marked portion in the 3D surface diagram), and a new peak at 1600 cm⁻¹appeared at 55 min, corresponding to the desired product (pink line, Fig. 3), and its peak intensity increased significantly with time. Although the decreasing portion and the increasing portion were found to be merged, the distinct nature of these two peaks was understood to a considerable extent (Supporting Information).



Figure 3. FTIR spectra of individual reaction partners

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Figure 4. Mid-IR-ATR 3D surface of the ongoing reaction

The formation of symmetrical bisindolyltriarylmethane (5 in Table 1) as a side product encouraged us to examine it in the formation of a new series of synthons, 2,2-di(1*H*-indol-3-yl)-1-phenylethanone derivatives (**5a-c**, Scheme 5) starting from phenyl glyoxal and indole (excess) using Cu(OTf)₂ catalyst (5mol%) in dioxane, utilized *in situ* for the construction of complex indolocarbazole analogues. To our delight, under similar reaction conditions, a new class of 2,2-di(1*H*-indol-3-yl)-1-phenylethanone and its bromo- and methoxy derivatives (**5b-d**) were rapidly (15 min-2 h) synthesized with excellent yield (82-91%).

Scheme 5. Synthesis of bisindolylbenzoylmethanes (5)



We designed and synthesized bisindolylbenzoylmethanes for the construction of two new series of complex carbazole compounds (Scheme 6) possessing both electron-rich (e.g., indole) and electron-deficient (e.g., benzoyl) moieties, which are innovative organic materials for the fabrication of a new generation of organic electronic devices of ultimate sensitivity. The formation of these bisindolyltriarylmethanes (5a, Scheme 3) prompted us to construct 2,2-di(1H-indol-3-yl)-1-phenylethanone (III, Scheme 6) utilizing α -ketoaldehyde (2n). We envisioned that the condensation of 5 with substrate 7 (III, path a) bearing an active ketomethylene group would provide the complex carbazole 8 possessing an indole substituent. The mechanism for construction of compound 9 is unknown to us. However it expected that in the presence of Cu^{II}-catalyst under oxidative condition, the robust cyclization catalysis was carried out through the tandem functionalization of two sp²C-H groups with the oxidative coupling of an active CH₂ (7, IV),^{1a} the release of sp³C-H and selective C-C cleavage leading to the construction of the valuable complex indolocarbazoles (9, path b). Both the indole-based carbazole compounds (8,9) are useful nanobuilding blocks possessing a wide range of gluing weak interactions such as H-bonding donor and acceptor, $\pi - \pi$ stacking, van der Waals and dipole-dipole attractive interactions operating between nanobuilding blocks to offer selfaggregated organic nanomaterials.



Gratifyingly, the treatment of an assembly of precursors including indole (**1a**, 2.1 mmol)and phenyl glyoxal (**2n**, 1mmol) using $Cu(OTf)_2$ catalyst (5mol%) in dioxane at 80 °C (1 h) for the *in situ* generation of 2,2-di(1*H*-indol-3-yl)-1-phenylethanone (**5b**) and subsequent addition of 4,4,4-trifluoro-1-phenylbutane-1,3dione (**7a**, 1 mmol) and DMAP (1mmol) under oxygen-free (argon atmosphere) refluxing conditions (10 h) produced the desired multifold C-C coupled product, indole-bearing carbazoles **8a**, with 76% yield (Scheme 7). This multifold C-C coupling catalysis is also selective because the unsymmetrical ketomethylene compound (**7a**) did not occur to construct the other possible regioisomer **8b**. Herein, the strong carbonyl characteristic of the -COCF₃ moiety led to selective condensation with the indole-C₂ of **5b**, and thus **8b** was not detected in the post-reaction mixture.

Scheme 7. Selective Pseudo-Four Component Coupling Catalysis to Indole-Substituted-Carbazole



Next, we turn our attention to the more challenging synthesis of valuable symmetrical indolo[2,3-b] carbazoles (9, Scheme 8) through an oxidative multifold C-C coupling cyclization reaction. The selective synthesis of compound 9 over the more thermodynamically stable unsymmetrical isomer indolo[3.2-b]carbazoles (10) is a challenging goal, and we focused on testing various oxidants (I₂, DDQ, O₂, air and Cu(OAc)₂.H₂O) and bases (K₂CO₃, piperidine, DMAP and DABCO) with changes in temperature (Supporting Information). Among the different bases, DABCO (20mol%) was found to be efficient in combination with aerial oxygen as a stoichiometric oxidant for the C-H functionalized cyclization process. Another noteworthy observation is that in no case was the corresponding non-oxidative multifold C-C coupling condensation product (8, Scheme 7) or isomeric byproduct 10 detected. With the optimized conditions in hand, we explored the synthesis of various 5,7-dihydroindolo[2,3-b]carbazole structures using indole, indole bearing electron-donating (5-OMe) and

Scheme 6. Multifold C-C Coupled Selective Cyclization Reactions

Scheme 8. Selective Synthesis of Indolo[2,3-*b*]carbzoles



tron-withdrawing (5-Br) substituents (1), phenylglyoxal (2n) and symmetrical active methylene compounds (7) such as acetylacetone (7b, entry 1), benzovlacetophenone (7c, entries 2,3,5), diethyl malonate (7d, entry 4), dimethyl malonate (7e, entry 6), 3,5-dioxoheptane (7f, entry 7), malononitrile (7g, entry 8) and N,N-diphenylmalonoamide (7h, entry 9). Herein, the pseudo-fourcomponent assembly rapidly passed through a domino oxidative cyclization catalysis through the formation of multiple C-C bonds to obtain valuable symmetrical functionalized indolo[2,3b]carbazoles (9a-i) with outstanding selectivity and good yield. These heterocycles possess both electron-donating and electronwithdrawing chromophores along with several weak attractive forces, making them potential nanobuilding blocks with gluing interactions to construct organic nanomaterials for innovative organic electronic applications. The structure of compound 9h was confirmed through analyses of single crystal X-ray diffraction data (CCDC no: 1508780; Supporting Information).

To shed light on the possible reaction pathways, we have performed control experiments for the two-step reaction (Scheme 9). In the first control experiment, phenylglyoxal (1mmol), indole (2.1mmol) and unsymmetrical 1,3-diketone PhCOCH₂COCF₃ were reacted under aerobic conditions. Surprisingly, a mixture of carbazoles was obtained (eq. vi, Scheme 9) with 48% of the condensation product (8a) along with 25% oxidative cyclization product (9b). This result clearly indicates that the strong carbonyl characteristic of $COCF_3$ (7a) led to the construction of the condensation product (8a) at a faster reaction rate even under oxidative reaction conditions (path a, Scheme 6). However, 1,3dicarbonyl compounds (7b-h, Scheme 8) bearing relatively less electrophilic carbonyl centers preferred to undergo an oxidative cyclization pathway even through C-C bond cleavage (path b, Scheme 6). We also investigated the oxidative cyclization reactions using unsymmetrical 1,3-dicarbonyl compounds (7i-l, eq. vii-x, Scheme 9), which produced a mixture of products in each case. The major ones contained relatively less electrophilic carbonyl moieties such as -CONHPh (9i, 51%, eq.vii) -CONHPh

Scheme 9. Control experiments under oxidative conditions





Oxidative Cyclization with Unsymmetrical 1,3-Dicarbonyl Compound

Oxidative Cyclization with a Mixture of Activated and Deactivated Indole



(9i, 54%, eq. viii), -COPh (9b, 45%, eq. ix) and -CN (9h, 70%, eq. x), compared to -COPh (9b, 23%), COMe (9a, 15%), COMe (9a, 23%) and CO₂Et (9d, 1%), respectively. From these results, it can be concluded that the selective nucleophilic attack of the DABCO on the more electrophilic carbon of the active methylene compound is crucial to achieve the major product. Thus, cleavage of the C-C bond for removal of the second carbonyl moiety may be considered as the rate determining transition state. However, this reaction was completely arrested in the absence of molecular oxygen or air, which verifies the necessity of oxidant for the three C-H bond-activated cyclization. To understand the influence of activated and deactivated indole in the reaction, we conducted a reaction (eq. xi) using phenyl glyoxal (2n, 1mmol), 5methoxyindole (1i, 2mmol), 5-bromoindole (1j, 2mmol) and 1,3diphenylpropane-1,3-dione (7c, 1mmol) under the developed reaction conditions. Surprisingly, the product incorporating two 5methoxyindolegroups 9c was found as the exclusive product (65%) alongside a negligible amount of the 1i and 1j insertion product 9j. We were unable to detect the third possible product 9k with both 5-bromoindoles relatively deactivated (1j). Thus, the reaction is more favorable for activated indoles.

Based on ESI-MS analysis data of the ongoing multifold C-C coupling cyclization reaction, the possible mechanism is depicted in Scheme 10. Formation of the bisindolylbenzoylmethane (I-3) intermediate was confirmed by the m/z [M+Na] symbolic peak in the ESI-MS spectra (Supporting Information). It is expected that the cyclization reaction should pass through the first C-C coupling between the activated sp³C-H of 7c and one of the sp²C₂-H groups^{1a} of the two indole residues with powerful Cu^{II}-catalyst under oxidative conditions, followed by coupling with the other sp²C₂-H. Both intermediates I-4 and I-5 were detected in the ESI-MS experiment (Supporting Information). In the final step, DABCO mediated C-C cleavage of I-5 with oxidation to afford the desired product 9b.

Scheme 10. Plausible Reaction Pathway for Oxidative Multifold C-C Coupling



CONCLUSION

We have demonstrated a three-component coupling method for selective synthesis of unsymmetrical indolo-triarylmethanes using readily available aldehydes, indoles and arylboronic acids as well as bisindolylarylmethanes through Cu^{II}-catalyzed dual C-C coupling. This novel strategy is advantageous in terms of easily available inexpensive precursors, simplicity of execution, large substrate scope, excellent functional group tolerance, a wide range of indole-based new compounds, chemo-, regio- and product selectivity and high yields. We have also found useful reaction insights through several control experiments, 3D mid-IR-ATR and mass spectra analysis of the ongoing reaction as well as DFT study for the crucial transition state. The development of a robust catalysis approach to diverse C-C coupling reactions and the synthesis of indole-based functionalized molecules is expected to find considerable application in organic synthesis, medicinal chemistry and material science.

EXPERIMENTAL SECTION

General Methods. All reagents were purchased from commercial suppliers and used without further purification. Petroleum ether used in our experiments was in the boiling range of 60-80 °C. Column chromatography was performed on silica gel (100-200 mesh and 230-400 mesh). Reported melting points are uncorrected. ¹H NMR and ¹³C NMR spectra were recorded at ambient temperature in CDCl₃/DMSO-*d*₆solution. Chemical shift are reported in ppm (δ) relative to internal reference tetramethylsilane. Coupling constants are quoted in Hz (*J*). Proton multiplicities are represented as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), and m (multiplet). Splitting patterns that could not be interpreted were designated as multiplet (m). Infrared spectra were acquired by electron spray ionization technique on a Q-

tof-micro quadriple mass spectrophotometer. X-RAY crystallographic data was taken using an X-ray diffractometry instrument.

General Procedure for Synthesis of Indolyltriarylmethane (GP-I) 4a-r.To a mixture of arylboronic acid (1.2 mmol), indole (1.2 mmol), aldehyde (1 mmol) and Cu(OTf)₂ (5 mol%),dioxane (3 mL) was added and stirred at 80 °C under air to complete the reaction, which was monitored by TLC. Dioxane was removed from the reaction mixture and extracted with ethyl acetate. The combined organic phase was washed with brine, dried on activatedNa₂SO₄and concentrated in a rotary evaporator under reduced pressure at ambient temperature. The residue was purified by silica gel column chromatography using suitable eluent to afford the desired product.

3-(Phenyl(*p***-tolyl)methyl)-1***H***-indole (4a). The compound was prepared following the GP-I** employing 4-methylbenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (3% pet ether-acetone) afforded the title compound as reddish brown solid (234 mg, 0.79 mmol, 79% yield).**M.P.** 78-80 °C; ¹**H NMR** (300 MHz, CDCl₃): δ 2.30 (s, 3H), 5.61 (s, 1H), 6.51 (d, *J*= 1.2 Hz,1H), 6.93-7.30 (m, 13H), 7.84 (brs, 1H); ¹³**C NMR** (125 MHz, CDCl₃): δ 21.2, 48.6, 111.2, 119.5, 120.1, 120.2, 122.2, 124.1, 126.3, 127.2, 128.4, 129.0, 129.1, 135.8, 136.8, 141.1, 144.3;**FT-IR** (KBr, cm⁻¹): 1094.8, 1415.3, 1456.1, 1492.7, 1511.0, 1642.6, 3418.5;**HRMS** (ESI-TOF) m/z Calcd for C₂₂H₁₈N [M-H]: 296.1439, found 296.1468.

2-((1*H*-Indol-3-vl)(phenvl)methvl)phenol (4b).¹⁸ The compound following the GP-I was prepared employing 2hydroxylbenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (15% pet ether-acetone) afforded the title compound as brown solid (209.3 mg, 0.70 mmol, 70% yield). M.P. 76-78 °C; ¹H NMR (300 MHz, CDCl₃): δ 5.09 (brs, 1H), 5.82 (s, 1H), 6.64 (d, J= 2.1 Hz, 1H), 6.81-6.85 (m, 2H), 6.92-7.02 (m, 2H), 7.11-7.35 (m, 9H), 8.02 (brs, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 43.3, 111.2, 116.3, 117.7, 119.7, 119.8, 120.8, 122.5, 124.0, 126.7, 126.9, 128.0, 128.6, 1129.0, 129.7, 130.1, 136.9, 142.3, 153.9; **FT-IR** (KBr, cm⁻¹): 699.0, 742.3, 1090.9, 1454.0, 1591.9, 2922.5, 3413.1.

3-((4-Nitrophenyl)(phenyl)methyl)-1*H***-indole (4c).** The compound was prepared following the **GP-I** employing 4nitrobenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (15% pet ether-acetone) afforded the title compound as deep yellow solid (233 mg, 0.71 mmol, 71% yield). **M.P.** 89-91 °**C**; ¹**H NMR** (300 MHz, CDCl₃): δ 5.79 (s, 1H), 6.59 (s, 1H), 7.05 (t, *J*= 7.5 Hz, 1H), 7.20-7.29 (m, 4H), 7.32-7.35 (m, 3H), 7.38-7.43 (m, 2H), 8.15 (d, *J*= 8.7 Hz, 3H); ¹³**C NMR** (75 MHz, CDCl₃): δ 48.6, 111.3, 118.2, 119.4, 119.6, 122.4, 123.5, 124.1, 126.4, 126.8, 128.6, 128.8, 129.8, 136.6, 142.3, 146.4, 151.6; **FT-IR** (KBr, cm⁻¹): 701.6, 473.0, 1097.1, 1343.8, 1516.3, 1593.9, 3414.3; **HRMS** (ESI-TOF) m/z Calcd for C₂₁H₁₅N₂O₂ [M-H]: 327.1134, found 327.1128.

3-((4-Methoxyphenyl)(phenyl)methyl)-1*H***-indole (4d).¹⁹ The compound was prepared following the GP-I** employing 4nitrobenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (20% pet ether-DCM) afforded the title compound as sticky liquid (241 mg, 0.77 mmol, 77% yield). ¹**H NMR** (300 MHz, CDCl₃): δ 3.73 (s, 3H), 5.57 (s, 1H), 6.49 (s, 1H), 6.77 (d, *J*= 8.7 Hz, 2H), 6.94 (t, *J*= 7.5 Hz, 1H), 7.08-7.30 (m, 9H), 7.88 (brs, 1H); ¹³C **NMR** (75 MHz, CDCl₃): δ 48.0, 55.2, 111.0, 113.6, 119.4, 120.0, 122.1, 124.0, 126.1, 127.0, 128.3, 128.9, 129.9, 136.2, 136.7, 144.3, 158.0; **FT-IR** (Neat, cm⁻¹): 1031.8, 1246.7, 1456.0, 1509.3, 1599.9, 3420.1.

3-((2-Nitrophenyl)(phenyl)methyl)-1*H***-indole (4e).** The compound was prepared following the **GP-I** employing 4nitrobenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (15% pet ether-acetone) afforded the title compound as deep yellow solid (230 mg, 0.70 mmol, 70% yield). **M.P.** 153-155 °C; ¹**H NMR** (300 MHz, CDCl₃): δ 6.40 (s, 1H), 6.51 (s, 1H), 6.96-7.01 (m, 1H), 7.14-7.41 (m, 11H), 7.85 (dd, *J*= 7.8 Hz, 1.2 Hz, 1H), 8.01 (brs, 1H); ¹³**C NMR** (75 MHz, CDCl₃): δ 43.3, 111.2, 118.3, 119.5, 119.7, 122.4, 124.4, 124.5, 126.6, 126.7, 127.4, 128.4, 129.0, 131.5, 132.4, 136.8, 137.9, 141.8, 149.8; **FT-IR** (KBr, cm⁻¹): 747.1, 1357.6, 1456.7, 1514.9, 1521.8, 2853.4, 2924.2, 3420.0; **HRMS** (ESI-TOF) m/z Calcd for C₂₁H₁₅N₂O₂ [M-H]: 327.1133, found 327.1112.

3-((4-Fluorophenyl)(phenyl)methyl)-5-nitro-1H-indole (4f). The compound was prepared following the GP-I employing 4fluorobenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and 5-nitroindole (1.2 mmol). Purification by column chromatography (10% pet ether-EtOAc) afforded the title compound as yellow solid (225 mg, 0.65 mmol, 65% yield). M.P. 246-248 °C; ¹H **NMR** (300 MHz, CDCl₃+DMSO- d_6): δ 5.68 (s, 1H), 6.73 (s, 1H), 6.97 (t, J= 8.4 Hz, 2H), 7.15-7.31 (m, 7H), 7.41 (d, J= 9.0 Hz, 1H), 7.99 (d, J= 9.0 Hz, 1H), 8.10 (s, 1H), 11.04 (brs, 1H); ¹³C NMR (75 MHz, CDCl₃+DMSO-d₆): δ 47.0, 111.0, 114.4, 114.7, 116.2 (d, J= 40.6 Hz, <u>C</u>-CF), 120.5, 125.4, 126.0, 127.2, 127.9, 128.1, 129.6, 129.7, 139.7, 140.3, 140.6 (d, *1J* = 294.8 Hz, <u>CF</u>), 162.4; **FT-IR** (KBr, cm⁻¹): 700.4, 740.5, 1089.0, 1232.7, 1321.5, 1506.0, 2356.3, 2923.7, 3291.9; HRMS (ESI-TOF) m/z Calcd for C₂₁H₁₆FN₂O₂ [M+H]: 347.1196, found 347.1192.

3-((4-Nitrophenyl)(o-tolyl)methyl)-1*H***-indole (4g).** The compound was prepared following the **GP-I** employing 4nitrobenzaldehyde (1 mmol), 2-methylphenylboronic acid (1.2 mmol) and 5-nitroindole (1.2 mmol). Purification by column chromatography (10% pet ether-EtOAc) afforded the title compound as sticky liquid (229 mg, 0.67 mmol, 67% yield). ¹**H NMR** (300 MHz, CDCl₃): δ 2.32 (s, 3H), 5.93 (s, 1H), 6.48 (d, *J*= 1.5 Hz, 1H), 6.91 (d, *J*= 7.5 Hz, 1H), 7.01-7.14 (m, 2H), 718-7.29 (m, 4H), 7.35-7.42 (m, 3H), 8.07-8.16 (m, 3H); ¹³**C NMR** (75 MHz, CDCl₃): δ 19.7,45.0, 111.3, 117.9, 119.4, 119.7, 122.5, 124.0, 124.3, 126.2, 126.7, 126.9, 128.8, 130.0, 130.7, 136.3, 136.8, 140.6, 146.6, 151.4; **FT-IR** (Neat, cm⁻¹): 1345.4, 1596.4, 1604.6, 1655.0, 3418.5; **HRMS** (ESI-TOF) m/z Calcd for C₂₂H₁₉N₂O₂[M+H]: 343.1447, found: 343.1472.

2-Methyl-3-((4-nitrophenyl)(phenyl)methyl)-1*H***-indole (4h). The compound was prepared following the GP-I** employing 4nitrobenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and 2-methylindole (1.2 mmol). Purification by column chromatography (10% pet ether-EtOAc) afforded the title compound as thickliquid (222 mg, 0.65 mmol, 65% yield). ¹**H NMR** (300 MHz, CDCl₃): δ 2.11 (s, 3H), 5.73 (s, 1H), 6.83-6.89 (m, 2H), 6.98-7.04 (m, 1H), 7.11-7.13 (m, 2H), 7.17-7.30 (m, 6H), 7.91 (brs, 1H), 8.04 (d, *J*= 8.7 Hz, 2H); ¹³C **NMR** (75 MHz, CDCl₃): δ 12.4, 47.8,110.5, 112.6, 119.1, 119.5, 121.2, 123.5, 126.7, 127.9, 128.6, 129.0, 130.0, 132.4, 135.3, 142.2, 146.4, 151.9; **FT-IR** (Neat, cm⁻¹): 746.7, 1344.9, 1459.7, 1517.1, 1594.4, 1705.8, 3403.6; **HRMS** (ESI-TOF) m/z Calcd for C₂₂H₁₉N₂O₂[M+H]: 343.1447, found: 343.1470.

5-Bromo-3-((4-nitrophenyl)(phenyl)methyl)-1H-indole (4i). The compound was prepared following the **GP-I** employing 4nitrobenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and 5-bromolindole (1.2 mmol). Purification by column chromatography (5% pet ether-EtOAc) afforded the title compound as thick liquid (256 mg, 0.63 mmol, 63% yield). ¹H NMR (300 MHz, CDCl₃): δ 5.70 (s, 1H), 6.59 (s, 1H), 7.16-7.22 (m, 2H), 7.27-7.38 (m, 7H), 8.13-8.16 (m, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 48.4, 112.8, 113.0, 118.1, 121.9, 123.7, 125.3, 125.4, 127.0, 128.3, 128.7, 128.8, 129.6, 129.7, 135.3, 141.9, 146.7, 151.1; FT-IR (Neat, cm⁻¹): 1345.0, 1451.9, 1518.1, 1587.4, 3412.2; HRMS (ESI-TOF) m/z Calcd for due C₂₁H₁₆BrN₂O₂ [M+H]: 407.0395, found 405.0368, 407.0373.

5-Methoxy-3-((4-nitrophenyl)(phenyl)methyl)-1*H***-indole (4j).** The compound was prepared following the GP-I employing 4-nitrobenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and 5-methoxylindole (1.2 mmol). Purification by column chromatog-raphy (8% pet ether-EtOAc) afforded the title compound as thick-liquid (272 mg, 0.76 mmol, 76% yield). ¹H NMR (300 MHz, CDCl₃): δ 3.68 (s, 3H), 5.72 (s, 1H), 6.57 (dd, *J*= 2.4 Hz, 9.9 Hz, 2H), 8.86 (dd, *J*= 2.4 Hz, 8.7 Hz, 1H), 7.20-7.33 (m, 6 H), 7.40 (d, *J*= 8.7 Hz, 2H), 8.03 (brs, 1H), 8.14 (d, *J*= 8.7 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 48.7, 55.8, 101.6, 112.0, 112.3, 118.0, 123.6, 124.8, 126.9, 127.0, 128.6, 128.9, 129.8, 131.9, 142.3, 146.5, 151.6, 154.0; FT-IR (Neat, cm⁻¹): 1208.4, 1345.2, 1519.5, 1627.2, 3434.2; HRMS (ESI-TOF) m/z Calcd for C₂₂H₁₉N₂O₃ [M+H]: 359.1396, found 397.1428.

3-(Phenyl(pyren-4-yl)methyl)-1*H***-indole (4k).** The compound was prepared following the **GP-I** employing pyrene-4carbaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (5% pet ether-EtOAc) afforded the title compound as deep yellow solid (256 mg, 0.63 mmol, 63% yield). **M.P.** 77-79 °C; ¹**H NMR** (300 MHz, CDCl₃): δ 6.43 (s, 1H), 6.76 (s, 1H), 6.96-7.01 (m, 1H), 7.17-7.38 (m, 8H), 7.69-7.71 (m, 1H), 7.93-8.05 (m, 6H), 8.13-8.18 (m, 2H), 8.39 (d, *J*= 9.3, 1H); ¹³**C NMR** (75 MHz, CDCl₃): δ 45.0, 111.1, 115.2, 119.4, 119.8, 120.1, 120.6, 122.2, 123.6, 124.7, 124.9, 125.0, 125.1, 125.8, 126.3, 126.9, 127.0, 127.1, 127.5, 128.4, 128.8, 129.3, 129.6, 130.0, 130.2, 130.7, 131.3, 136.7, 137.6, 143.9; **FT-IR** (KBr, cm⁻¹): 713.5, 841.1, 1417.0, 1455.0, 2852.3, 2922.9, 3458.5; **HRMS** (ESI-TOF) m/z Calcd for C₃₁H₂₁NNa [M+Na]: 430.1572, found 430.1605.

3-(Phenyl(4-(trifluoromethyl)phenyl)methyl)-1*H***-indole (41). The compound was prepared following the GP-I** employing 4-(trifluoromethyl)benzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (8% pet ether-EtOAc) afforded the title compound as light brown solid (284 mg, 0.81 mmol, 81% yield). **M.P.** 112-114°C; ¹**H NMR** (300 MHz, CDCl₃): δ 5.69 (s, 1H), 6.49 (d, *J*= 1.2 Hz, 1H), 6.98 (t, *J*= 7.5 Hz, 1H), 7.13-7.32 (m, 10H), 7.50 (d, *J*= 8.1 Hz, 2H), 7.94 (brs, 1H); ¹³C **NMR** (75 MHz, CDCl₃): δ 48.7, 111.3, 115.3, 119.0, 119.6, 119.7, 122.4, 125.27, 125.30 (q, *IJ* = 225.0 Hz, <u>CF₃</u>), 125.32, 126.8, 128.5, 128.8, 129.0, 129.4, 136.7, 143.0, 148.1; **FT-IR** (KBr, cm⁻¹): 743.8, 805.8, 1067.2, 1108.2, 1165.1, 1323.9, 3424.0; **HRMS** (ESI-TOF) m/z Calcd for C₂₂H₁₅F₃N [M-H]: 350.1157, found 350.1167.

3-(Naphthalen-1-yl(phenyl)methyl)-1*H***-indole (4m).** The compound was prepared following the **GP-I** employing 1naphthaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (2% pet ether-EtOAc) afforded the title compound as brown solid (200 mg, 0.60 mmol, 60% yield). **M.P.** 68-70 °C; ¹**H NMR** (300 MHz, CDCl₃): δ 6.45 (d, *J*= 4.5 Hz, 2H),7.00-7.05 (m, 1H), 7.13-7.50 (m, 12H), 7.78 (d, *J*= 8.1 Hz, 1H), 7.90 (d, *J*= 7.8 Hz, 2H), 8.14 (d, *J*= 8.1 Hz, 1H); ¹³C **NMR** (75 MHz, CDCl₃): δ 44.7, 111.1, 115.3, 119.5, 119.8, 122.2, 124.3, 124.8, 125.4, 126.0, 126.3, 126.9, 127.0, 127.2, 128.4, 128.7, 129.3, 131.9, 134.0, 136.7, 139.6, 143.7; **FT-IR** (KBr, cm⁻¹): 1093.1, 1415.6, 1455.7, 1492.4, 1596.0, 3056.1, 3418.5; **HRMS** (ESI-TOF) m/z Calcd for C₂₅H₁₈N [M-H]: 332.1439, found 332.1416.

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59 60 **3-(Anthracen-9-yl(phenyl)methyl)-1***H***-indole (4n).** The compound was prepared following the **GP-I** employing anthracene-9carbaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (3% pet ether-EtOAc) afforded the title compound as brown solid (234 mg, 0.61 mmol, 61% yield). **M.P.** 84-86 °C; ¹**H NMR** (300 MHz, CDCl₃): δ 6.65 (s, 1H), 7.08-7.29 (m, 9H), 7.36-7.43 (m 3H), 7.48 (d, *J*= 7.8 Hz, 1H), 7.92 (brs, 1H), 8.03 (d, *J*= 8.4 Hz, 2H), 8.34 (d, *J*= 9.0 Hz, 2H), 8.47 (s, 1H); ¹³C **NMR** (75 MHz, CDCl₃): δ 41.7, 111.2, 119.6, 119.8, 122.2, 124.7, 125.3, 125.7, 125.9, 127.4, 127.9, 128.2, 128.5, 129.2, 130.5, 132.1, 136.4, 144.5; FT-IR (KBr, cm⁻¹): 704.6, 730.3, 1096.0, 1338.5, 1446.0, 1455.9, 1491.2, 2923.4, 3050.1, 3414.6; **HRMS** (ESI-TOF) m/z Calcd for C₂₉H₂₀N [M-H]: 382.1596, found 382.1622.

12 3-(Mesityl(phenyl)methyl)-1*H*-indole (40).²⁰ The compound was 13 following the GP-I employing prepared 2.4.6-14 trimethylbenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) 15 and indole (1.2 mmol). Purification by column chromatography 16 (5% pet ether-EtOAc) afforded the title compound as brown solid 17 (202 mg, 0.62 mmol, 62% yield). M.P. 45-47 °C;¹H NMR (300 18 MHz, CDCl₃): δ 2.09 (s, 6H), 2.31 (s, 3H), 6.13 (s, 1H), 6.63 (s, 19 1H), 6.87 (2H), 7.03-7.08 (m, 1H), 7.16-7.33 (m, 5H), 7.39 (d, J= 8.1 Hz, 1H), 7.96 (brs, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 20.9, 20 21.7, 42.9, 111.1, 116.8, 119.4, 119.9, 122.0, 123.9, 125.6, 127.8, 21 128.0, 128.9, 130.1, 135.7, 136.6, 137.3, 137.8, 143.4; FT-IR 22 (KBr, cm⁻¹): 741.1, 1093.2, 1149.3, 1337.1, 1455.8, 1491.9, 23 2916.9, 3413.4 24

3-((2-Bromophenyl)(phenyl)methyl)-1H-indole (4p). The com-25 pound was prepared following the GP-I employing 2-26 bromobenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) 27 and indole (1.2 mmol). Purification by column chromatography 28 (8% pet ether-EtOAc) afforded the title compound as brown solid 29 (235 mg, 0.65 mmol, 65% yield). M.P. 86-88 °C; ¹H NMR (300 30 MHz, CDCl₃): δ 6.05 (s, 1H), 6.45 (s, 1H), 6.45-7. 31 (m, 12H), 7.55 (d, J= 8.1 Hz, 1H), 7.92 (brs, 1H); ¹³C NMR (75 MHz, 31 CDCl₃): δ 47.9, 111.1, 115.3, 119.0, 119.5, 119.8, 122.2, 124.3, 32 125.1, 126.4, 127.3, 128.0, 128.3, 129.2, 129.6, 130.9, 133.0, 33 136.7, 142.4, 142.8; **FT-IR** (KBr, cm⁻¹): 700.2, 718.3, 741.3, 34 751.2, 1020.4, 1091.9, 1415.0, 1454.7, 3387.2, 3437.8; HRMS 35 (ESI-TOF) m/z Calcd for C₂₁H₁₇BrN [M+H]: 362.0544, found 36 360.0502, 362.0515.

3-(4-Methyl-1-phenylpentyl)-1*H***-indole (4q).**The compound was prepared following the GP-I employing 3-methylbutanal (1 mmol), phenylboronic acid (1.2 mmol) and indole (1.2 mmol). Purification by column chromatography (5% pet ether-EtOAc) afforded the title compound as brown solid (158 mg, 0.60 mmol, 60% yield). M.P. 80-82 °C; ¹H NMR (300 MHz, CDCl₃): δ 0.88-0.91 (m, 3H), 0.95-0.98 (m, 3H), 1.47-1.56 (m, 1H), 1.88-2.06 (m, 2H), 4.25-4.30 (m, 1H), 6.95-7.03 (m, 2H), 7.09-7.15 (m, 2H), 7.20-7.31 (m, 5H), 7.47 (d, *J*= 7.8 Hz, 1H), 7.86 (brs, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 22.4, 23.2, 25.6, 40.4, 45.6, 111.0, 119.2, 119.4, 120.6, 121.0, 121.9, 125.9, 127.1, 127.9, 128.3, 136.5, 145.6; FT-IR (KBr, cm⁻¹): 701.0, 740.9, 1456.9, 2951.2, 3411.5; HRMS (ESI-TOF) m/z Calcd for C₁₉H₂₂N [M+H]: 264.1752, found 264.1780

1-Methyl-3-(phenyl(*p***-tolyl)methyl)-1***H***-indole (4r). The compound was prepared following the GP-I** employing 4-methylbenzaldehyde (1 mmol), phenylboronic acid (1.2 mmol) and 1-methylindole (1.2 mmol). Purification by column chromatography (0.5% pet ether-EtOAc) afforded the title compound as brown solid (171 mg, 0.55 mmol, 55% yield). **M.P.** 78-80 °C; ¹**H NMR** (300 MHz, CDCl₃): δ 2.31 (s, 3H), 3.68 (s, 3H), 5.62 (s, 1H), 6.40 (s, 1H), 6.94-6.99 (m, 1H), 7.06-7.16 (m, 4H), 7.19-7.29 (m, 8H); ¹³C **NMR** (75 MHz, CDCl₃): δ 20.2, 31.8, 47.5, 108.2, 117.6, 117.9, 119.1, 120.7, 125.2, 126.5, 127.4, 127.8, 128.0, 128.1, 134.7, 136.6, 140.3, 143.5; **FT-IR** (KBr, cm⁻¹):

1116.0, 1228.2, 1329.0, 1370.2, 1469.4, 1510.2, 2853.4, 2923.8; **HRMS** (ESI-TOF) m/z Calcd for $C_{23}H_{20}N$ [M-H]: 310.1596, found 310.1623.

General Procedure for Synthesis of 5a-d (GP-II). To a mixture of indole/substituted indole (2.0 mmol), 4methylbenzaldehyde/phenyl glyoxal (1.0 mmol) and Cu(OTf)₂ (5 mol%), dioxane (4 mL) was added and stirred at 80 °C under air to complete the reaction, which was monitored by TLC. Dioxane was removed from the reaction mixture and extracted with ethyl acetate. The combined organic phase was washed with brine, dried on activated Na₂SO₄ and concentrated in a rotary evaporator under reduced pressure at ambient temperature. The residue was purified by silica gel column chromatography using suitable eluent to afford the desired product5.

3,3'-(*p***-Tolylmethylene)***bis***(1***H***-indole) (5a).²¹ ¹H NMR (300 MHz, CDCl₃): \delta 2.22 (s, 3H), 5.74 (s, 1H), 6.47 (d, 2H,** *J***= 1.5 Hz), 6.87-6.93 (m, 2H), 6.98 (d,** *J***= 7.1 Hz, 2H), 7.03-7.14 (m, 4H), 7.20 (d,** *J***= 7.1 Hz, 2H), 7.29 (d,** *J***= 7.1 Hz, 2H), 7.65 (brs, 2H); ¹³C NMR (75 MHz, CDCl₃): \delta 21.1, 39.7, 111.0, 119.1, 119.8, 119.9, 121.8, 123.5, 127.0, 128.5, 128.9, 135.5, 136.6, 141.0.**

2,2-Di(1*H***-indol-3-yl)-1-phenylethanone (5b).²²** The compound was prepared following **GP-II** employing indole (2.0 mmol), phenyl glyoxal (1.0 mmol) and Cu(OTf)₂ (5 mol%). Purification by column chromatography (DCM) afforded the title compound as red thick liquid (319 mg, 0.91 mmol, 91% yield). ¹**H NMR** (300 MHz, CDCl₃): δ 6.51 (s, 1H), 6.88 (s, 2H), 7.09 (d, *J*= 7.2 Hz, 2H), 7.18 (t, *J*= 7.2 Hz, 2H), 7.32 (d, *J*= 7.8 Hz, 2H), 7.38-7.43 (m, 2H), 7.50-7.57 (m, 3H), 8.07-8.12 (m, 4H); ¹³C NMR (75 MHz, CDCl₃): δ 42.1, 111.3, 114.2, 118.9, 119.7, 122.2, 124.0, 126.6, 128.6, 128.7, 128.8, 132.9, 136.5, 136.9, 198.6.

2,2-*Bis*(**5-bromo-1***H***-indol-3-yl)-1-phenylethanone** (**5c**). The compound was prepared following **GP-II** employing indole (2.0 mmol), phenyl glyoxal (1.0 mmol) and Cu(OTf)₂ (5 mol%). Purification by column chromatography (20% pet ether-EtOAc) afforded the title compound as red solid (417 mg, 0.82 mmol, 82% yield). M.P. 98-100 °C; ¹**H** NMR (300 MHz, CDCl₃): δ 6.28 (s, 1H), 6.52 (s, 2H), 6.92 (d, *J*= 8.7 Hz, 2H), 7.09 (d, *J*= 8.7 Hz, 2H), 7.30-7.35 (m, 2H), 7.43-7.47 (m, 1H), 7.57 (s, 2H), 8.01 (d, *J*= 8.1 Hz, 2H), 8.30 (s, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 42.2, 112.8, 112.9, 113.2, 121.2, 125.0, 125.4, 127.9, 128.8, 128.9, 133.5, 135.2, 136.1, 199.1; **FT-IR** (KBr, cm⁻¹): 794.0, 884.8, 1098.0, 1213.3, 1447.2, 1458.3, 1674.0, 2923.0, 3341.2, 3419.5; **HRMS** (ESI-TOF) m/z Calcd for C₂₄H₁₇Br₂N₂O [M+H]: 506.9708, found 506.9734, 508.9737, 510.9964.

2,2-*Bis*(5-methoxy-1*H*-indol-3-yl)-1-phenylethanone (5d). The compound was prepared following **GP-II** employing indole (2.0 mmol), phenyl glyoxal (1.0 mmol) and Cu(OTf)₂ (5 mol%). Purification by column chromatography (20% pet ether-EtOAc) afforded the title compound as red solid (349 mg, 0.85 mmol, 85% yield). **M.P.** 172-174 °C; ¹H **NMR** (300 MHz, DMSO-*d*₆): δ 3.72 (s, 6H), 6.37 (s, 1H), 6.67 (s, 2H), 6.80 (d, *J*= 8.7 Hz, 2H), 6.98 (s, 2H), 7.09 (d, *J*= 8.7 Hz, 2H), 7.39 (t, *J*= 7.5 Hz, 2H), 7.49 (d, *J*= 6.9 Hz, 1H), 8.11 (d, *J*=7.5 Hz, 2H), 8.23 (s, 2H); ¹³C **NMR** (75 MHz, DMSO-*d*₆): δ 42.4, 55.8, 101.0, 111.9, 112.2, 113.2, 125.1, 126.8, 128.6, 128.7, 121.8, 132.9, 136.9, 153.9, 199.2; **FT-IR** (KBr, cm⁻¹): 685.8, 787.6, 1024.4, 1076.1, 1169.2, 1175.3, 1210.4, 1246.7, 1290.1, 1450.3, 1486.5, 1668.4, 2930.4, 3334.1, 3419.0; **HRMS** (ESI-TOF) m/z Calcd for C₂₆H₂₂NaN₂O₃ [M+Na]: 433.1528, found 433.1529.

Procedure for the Synthesis of 4-(1H-indol-3-yl)-3-phenyl-1-(trifluoromethyl)-9*H*-carbazol-2-yl)(phenyl)methanone (8a). To a mixture of indole (2.1 mmol), phenyl glyoxal (1mmol) and Cu(OTf)₂ (5 mol%), dioxane(4 mL) was added and heated at 80 °C for 15 min for in situ generation of 2,2-di(1H-indol-3-yl)-1phenylethanone (5b). 4,4,4-Trifluoro-1-phenylbutane-1,3-dione (1 mmol) and DMAP (1mmol) were added and refluxed under argon atmosphere for 10h (Scheme 7). The reaction mixture was extracted with ethyl acetate. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using 5% pet ether-EtOAc as an eluent to afford 8a (403 mg, 0.76 mmol, 76% yield).Deep yellow solid, M.P. 250-205 °C (decomposed); ¹H NMR (300 MHz, CDCl₃): δ 6.45 (d, J= 8.1 Hz, 1H), 6.76 (t, J= 7.5 Hz, 1H), 7.26-7.33 (m, 1H), 7.45-7.53 (m, 4H), 7.61-7.82 (m, 7H), 7.97-8.01 (m, 3H), 8.30 (q, J= 8.4 Hz, J= 12.0 Hz, 2H), 9.07 (s, 1H), 10.88 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): *δ* 111.0, 119.6, 119.8, 121.5, 121.6, 122.2, 122.3, 125.67, 125.72, 125.9, 127.3, 127.9, 128.4, 128.7, 128.8 (q, *1J*= 240.5 Hz, CF₃), 129.1, 129.7, 130.0, 132.6, 138.4, 138.9, 139.6, 142.8, 142.9, 158.2, 198.0; FT-IR (KBr, cm⁻¹): 1225.4, 1101.9, 1610.8, 1634.6, 2852.8, 2924.4, 3402.9; HRMS (ESI-TOF) m/z Calcd for due C₃₄H₂₂F₃N₂O [M+H]: 531.1684, found 531.1680.

General Procedure for Synthesis of 9a-i (GP-III). To a mixture of indole derivative (2.0 mmol), phenyl glyoxal (1.0 mmol) and Cu(OTf)₂ (5 mol%), dioxane (4 mL)was added and stirred at 80 °C for 15 min-2h depending on the substrate. Next, active methylene compound (1.0 mmol) and DABCO (20 mol%) were added to the reaction mixture and refluxed for the specified time under air. The reaction mixture was extracted with ethyl acetate. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using appropriate eluent to give the desired product.

1-(12-Benzoyl-5,7-dihydroindolo[2,3-*b***]carbazol-6-yl)ethanone (9a). The compound was prepared following GP-III employing phenyl glyoxal (1 mmol), indole (2.1 mmol) and acetylacetone (1 mmol). Purification by column chromatography (10% pet ether-EtOAc) afforded the title compound as deep yellow solid (289 mg, 0.72 mmol, 72% yield). M.P. 210-212 °C (decomposed); ¹H NMR (300 MHz, DMSO-***d***₆): δ 3.11 (s, 3H), 6.98-7.03 (m, 2H), 7.30-7.38 (m, 4H), 7.52 (t,** *J***= 7.5 Hz, 2H), 7.66-7.79 (m, 3H), 7.96 (d,** *J***= 7.2 Hz 2H), 11.64 (brs, 2H); ¹³C NMR (75 MHz, DMSO-***d***₆): δ 31.8, 103.9, 111.8, 113.7, 119.4, 120.0, 124.7, 128.9, 129.1, 132.0, 134.5, 135.0, 138.5, 140.3, 196.3, 197.3; FT-IR (KBr, cm⁻¹): 723.9, 1202.5, 1233.5, 1321.5, 1463.9, 1577.9, 1593.2, 1642.5, 2853.4, 2924.3, 3342.3, 3390.3; HRMS (ESI-TOF) m/z Calcd for C₂₇H₁₈N₂NaO₂ [M+Na]: 425.1266, found 425.1264.**

(5,7-Dihydroindolo[2,3-b]carbazole-6,12-

diyl)*bis*(phenylmethanone) (9b). The compound was prepared following GP-III employing phenyl glyoxal (1 mmol), indole (2.1 mmol) and 1,3-diphenylpropane-1,3-dione (1 mmol). Purification by column chromatography (10% pet ether-EtOAc) afforded the title compound as deep yellow solid (334 mg, 0.74 mmol, 74% yield). M.P. 178-180 °C; ¹H NMR (300 MHz, DMSO-*d*₆): δ 7.01-7.07 (m, 2H), 7.26-7.31 (m, 4H), 7.46 (t, *J*= 7.5 Hz, 2H), 7.53-7.56 (m, 2H), 7.59-7.66 (m, 3H), 7.71-7.74 (m, 1H), 7.82-7.86 (m, 2H), 8.12 (d, *J*= 7.5 Hz, 2H), 9.31 (brs, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 102.3, 110.8, 115.3, 120.6, 121.3, 121.4, 125.5, 128.0, 129.3, 129.5, 130.1, 132.3, 134.3, 134.6, 136.0, 139.6, 140.1, 140.9, 195.3, 197.6; FT-IR (KBr, cm⁻¹): 687.3, 707.0, 968.6, 727.5, 746.9, 1214.1, 1235.9, 1321.1, 1449.1, 1460.2, 1595.4, 1630.4, 1668.1, 2852.2, 2922.8, 3362.3, 3445.7;

HRMS (ESI-TOF) m/z Calcd for $C_{32}H_{21}N_2O_2$ [M+H]: 465.1603, found 465.1596.

(2,10-Dibromo-5,7-dihydroindolo[2,3-b]carbazole-6,12-

diyl)*bis*(phenylmethanone) (9c). The compound was prepared following **GP-III** employing phenyl glyoxal (1 mmol), 5bromoindole (2.1 mmol) and 1,3-diphenylpropane-1,3-dione (1 mmol). Purification by column chromatography (20% pet ether-EtOAc) afforded the title compound as deep yellow solid (404 mg, 0.65 mmol, 65% yield). **M.P.** 300-303 °C (decomposed). ¹**H NMR** (300 MHz, DMSO-*d*₆): δ 7.49-7.55 (m, 5H), 7.64 (t, *J*= 7.5 Hz, 5H), 7.78-7.81 (m, 2H), 7.99-8.05 (d, *J*= 7.5 Hz, 2H), 8.11 (d, *J*= 7.2 Hz, 2H), 11.53 (s, 2H);¹³C **NMR** (75 MHz, DMSO-*d*₆): δ 103.6, 110.7, 112.9, 113.2, 121.8, 122.0, 127.4, 128.0, 128.5, 128.7, 129.1, 129.3, 129.5, 133.3, 134.85, 134.94, 136.8, 138.4, 139.3, 193.0, 196.8. **FT-IR** (KBr, cm⁻¹): 974.9, 1232.8, 1284.1, 1459.1, 1595.9, 1627.6, 1666.2, 2852.3, 2923.2, 3417.5.**HRMS** (ESI-TOF) m/z Calcd for C₃₂H₁₉Br₂N₂O₂ [M+H]: 620.9813, found 620.9805, 622.9797, 624.9771.

Ethyl 12-benzoyl-5,7-dihydroindolo[2,3-*b***]carbazole-6carboxylate (9d).²² The compound was prepared following GP-III employing phenyl glyoxal (1 mmol), 5-bromoindole (2.1 mmol) and diethylmalonate (1 mmol). Purification by column chromatography (8% pet ether-EtOAc) afforded the title compound as deep yellow solid (285 mg, 0.66 mmol, 66% yield). ¹H NMR (300 MHz, DMSO-***d***₆): \delta 1.57 (t,** *J***= 7.2 Hz, 3H), 4.75 (q,** *J***= 6.9 Hz, 14.1 Hz, 2H), 7.00-7.05 (m, 2H), 7.33-7.39 (m, 4H), 7.54 (t,** *J***= 7.5 Hz, 2H), 7.69-7.81 (m, 3H), 7.98 (d,** *J***= 7.2 Hz, 2H), 11.57 (s, 2H); ¹³C NMR (75 MHz, DMSO-***d***₆): \delta 14.3, 60.3, 93.6, 111.7, 113.1, 119.1, 119.3, 120.1, 124.7, 128.9, 129.1, 131.6, 134.5, 135.0, 138.9, 140.0, 165.6, 197.2; FT-IR (KBr, cm⁻¹): 695.4, 729.2, 1176.5, 1193.0, 1245.1, 1325.0, 1460.8, 1602.4, 1661.6, 1685.9, 2852.9, 2923.9, 3416.7.**

(2,10-Dimethoxy-5,7-dihydroindolo[2,3-b]carbazole-6,12-

diyl)bis(phenylmethanone) (9e). The compound was prepared following GP-III employing phenyl glyoxal (1 mmol), 5methoxyindole (2.1 mmol) and 1,3-diphenylpropane-1,3-dione (1 mmol). Purification by column chromatography (10% pet ether-EtOAc) afforded the title compound as deep yellow solid (356 mg, 0.68 mmol, 68% yield). M.P. 246-248 °C; ¹H NMR (300 MHz, CDCl₃): δ 3.63 (s, 6H), 6.92 (dd, *J*= 2.1 Hz, 9.0 Hz, 2H), 7.02 (s, 2H), 7.20 (d, *J*= 8.7 Hz, 1H), 7.47 (t, *J*= 7.5 Hz, 3H), 7.63 (t, *J*= 7.2 Hz, 4H), 7.82 (d, *J*= 6.9 Hz, 2H), 8.12 (d, *J*= 7.8 Hz, 2H), 9.18 (brs, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 55.7, 102.1, 104.7, 111.3, 114.0, 115.1, 121.8, 127.8, 129.3, 129.4, 129.9, 132.1, 134.3, 134.6, 136.1, 140.8, 154.2, 195.1, 197.8; FT-IR (KBr, cm⁻¹): 687.7, 1039.6, 1204.7, 1482.6, 1588.2, 2853.2, 2924.3, 3334.2, 3434.3; HRMS (ESI-TOF) m/z Calcd for C₃₄H₂₅N₂O₄ [M+H]: 525.1814, found 525.1852.

12-benzoyl-5,7-dihydroindolo[2,3-b]carbazole-6-Methyl carboxylate (9f). The compound was prepared following GP-III employing phenyl glyoxal (1 mmol), 5-methoxyindole (2.1 mmol) and dimethylmalonate (1 mmol). Purification by column chromatography (10% pet ether-EtOAc) afforded the title compound as deep yellow solid (280 mg, 0.67 mmol, 67% yield). M.P. 200-202 °C; ¹H NMR (300 MHz, DMSO- d_6): δ 4.23 (s, 3H), 7.04 (t, J= 7.5 Hz, 2H), 7.35-7.41 (m, 4H), 7.56 (t, J= 7.7 Hz, 2H), 7.74-7.82 (m, 3H), 8.0 (d, J= 3.6 Hz, 2H), 11.67 (s, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 51.6, 93.4, 111.7, 113.2, 119.2, 119.4, 120.1, 124.8, 128.1, 128.8, 129.0, 129.1, 132.4, 134.5, 135.0, 138.9, 140.1, 166.1, 197.3; **FT-IR** (KBr, cm⁻¹): 685.3, 729.0, 1082.8, 1173.9, 1206.1, 1245.1, 1324.5, 1601.5, 1659.6, 1687.7, 2852.8, 2923.7, 3416.3, 3433.2; HRMS (ESI-TOF) m/z Calcd for C₂₇H₁₈N₂NaO₃ [M+Na]: 441.1215, found 441.1213.

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59 60 1-(12-Benzoyl-5,7-dihydroindolo[2,3-b]carbazol-6-yl)propan-

1-one (9g). The compound was prepared following **GP-III** employing phenyl glyoxal (1 mmol), indole (2.1 mmol) and heptane-3,5-dione (1 mmol). Purification by column chromatography (10% pet ether-EtOAc) afforded the title compound as deep yellow solid (295mg, 0.71 mmol, 71% yield). **M.P.** 280-282 °C (decomposed). ¹**H NMR** (300 MHz, DMSO-*d*₆): δ 1.09-1.14 (m, 3H), 3.01-3.05 (m, 2H), 6.88-6.93 (m, 2H), 7.16-7.21 (m, 2H), 7.31-7.41 (m, 6H), 7.56 (t, *J*= 7.5 Hz, 1H), 7.99 (d, *J*= 7.5 Hz, 2H), 10.09 (s, 2H); ¹³**C NMR** (75 MHz, DMSO-*d*₆): δ 7.5, 36.9, 103.3, 111.0, 114.9, 120.4, 120.7, 120.9, 125.2, 129.2, 130.0, 132.6, 134.7, 135.8, 139.3, 139.8, 198.93, 198.99; **FT-IR** (KBr, cm⁻¹): 733.8, 1152.3, 1239.9, 1320.5, 1464.4, 1593.9, 1644.7, 2923.9, 3335.4, 3389.4; **HRMS** (ESI-TOF) m/z Calcd for C₂₈H₂₁N₂O₂ [M+H]: 417.1603, found 417.1576.

12-Benzoyl-5,7-dihydroindolo[2,3-b]carbazole-6-carbonitrile

(9h). The compound was prepared following GP-III employing phenyl glyoxal (1 mmol), indole (2.1 mmol) and malononitrile (1 mmol). Purification by column chromatography (15% pet ether-EtOAc) afforded the title compound as deep yellow solid (262 mg, 0.68 mmol, 68% yield). M.P. 296-290 °C; ¹H NMR (300 MHz, DMSO- d_6): δ 5.76-5.81 (m, 2H), 6.09-6.14 (m, 4H), 6.26-6.35 (m, 4H), 6.47 (t, J= 7.5 Hz, 2H), 6.72 (d, J= 7.5 Hz, 1H), 11.14 (s, 2H); ¹³C NMR (75 MHz, DMSO- d_6): δ 74.2, 111.2, 112.9, 115.2, 119.5, 119.6, 120.4, 125.2, 129.0, 129.1, 131.3, 134.6, 134.8, 140.1, 140.4, 196.7; FT-IR (KBr, cm⁻¹): 731.3, 1248.0, 1327.7, 1462.3, 1608.6, 1644.5, 2221.5, 2923.5, 3287.3, 3435.7; HRMS (ESI-TOF) m/z Calcd for C₂₆H₁₆N₃O [M+H]: 386.1293, found 386.1322.

12-Benzoyl-N-phenyl-5,7-dihydroindolo[2,3-b]carbazole-6-

carboxamide (9i). The compound was prepared following **GP-III** employing phenyl glyoxal (1 mmol), indole (2.1 mmol) and *N*,*N*diphenylmalonamide (1 mmol). Purification by column chromatography (8% pet ether-EtOAc) afforded the title compound as deep yellow solid (311 mg, 0.65 mmol, 65% yield). **M.P.** 80-82 °C; ¹**H NMR** (300 MHz, DMSO-*d*₆): δ 7.01 (t, *J*= 7.5 Hz, 2H), 7.22 (t, *J*= 7.2 Hz, 1H), 7.33-7.52 (m, 6H), 7.58 (t, *J*= 7.5 Hz, 2H), 7.66 (d, *J*= 8.1 Hz, 2H), 7.74 (d, *J*= 7.2 Hz, 1H), 8.01 (d, *J*= 4.5 Hz, 4H), 10.79 (s, 1H), 11.58 (s, 2H); ¹³C **NMR** (75 MHz, DMSO-*d*₆): δ 101.2, 111.1, 113.4, 118.5, 119.5, 120.1, 120.3, 123.1, 124.6, 127.8, 128.0, 128.3, 128.9, 129.0, 134.2, 135.4, 136.8, 139.1, 140.4, 164.1, 197.6; **FT-IR** (KBr, cm⁻¹): 689.9, 739.1, 1245.2, 1322.3, 1439.4, 1462.3, 1501.1, 1596.0, 1644.0, 2851.6, 2922.0, 3361.8; **HRMS** (ESI-TOF) m/z calcd for C₃₂H₂₂N₃O₂ [M+H]: 480.1712, found 480.1715.

ASSOCIATED CONTENT

Supporting Information

This material is available free of charge via the Internet at http://pubs.acs.org.

Materials and methods, optimization Table, general procedures, characterization data for all compounds, ¹H and ¹³C spectra of the new compounds, single crystal XRD data, and Mid-IR-ATR data and spectra.

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Notes

The authors declare no competing financial interests.

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