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Domino alkyne insertion/aldol reaction/aromatization of 2-alkynyl indole-3-carbaldehyde with 1,3-diketones: Entry to 2-indolyl phenols

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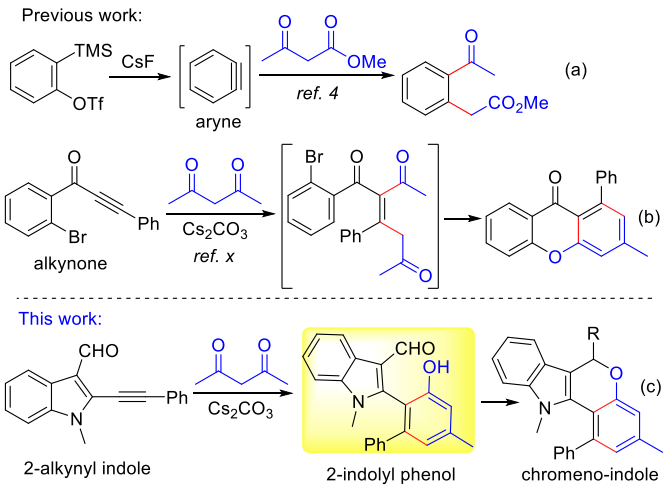
A novel one-pot base-promoted insertion of indolyl 2-alkynes into a C-C single bond of 1,3-diketones, followed by intramolecular aldol reaction and dehydrative aromatization is described. This reaction cascade leads to the construction of 2-indolyl phenols involving the formation of the C1-C2 and C3-C4 bonds of phenols resulting from the formal insertion process with a good substrate scope. Further, these bifunctional compounds were used in a novel arylative annulation in the presence of Grignard reagents to provide chromeno-indole frameworks.

Introduction

Insertion of alkynes (C-C triple bond) into carbon–carbon σ-bonds has been established as a powerful approach for the construction of various carbocyclic compounds involving the formation of two new C-C bonds.[1] Majority of these insertion reactions require transition-metal catalysed methods,[2] while some of them were accomplished under metal-free conditions.[3] In particular, the reactive alkynes such as arynes have been well explored for their insertion reactions in C-C single bonds without the use of transition-metals.[3-6] In 2005, for the first time Stolz's group observed the base-promoted insertion of an aryne into the α,β-single bond of a β-ketoester generating the arylketones (Scheme 1a) and benzannulated carbocycles.[4] Following this concept, a plethora of aryne insertion-based strategies have been developed towards heterocycles and carbocycles including bio-active natural products.[5] Furthermore, a few activated alkynes such as ynones also underwent the base-mediated insertion into C-C σ-bonds, leading to hetero- or carbo-cycles (Scheme 1b).[6] Herein, we disclose 2-alkynyl indole-3-carbaldehyde as a handy alkyne for an insertion reaction into the α,β-carbon-carbon single bond of 1,3-diketones under metal-free conditions leading to 2-indolyl phenols through a domino process. To the best of our knowledge, this type of domino approach to phenols comprising the insertion of indole-tethered alkyne is unprecedented. Further, the products were recognized as efficient precursors to construct new chromeno-indoles (Scheme 1c).

Notably, phenols play a crucial role in organic synthesis and constitute a privileged structural framework found in natural products, pharmaceuticals, polymers and many other areas.[7] Owing to their prominence, numerous methods have been developed over the years.[8-11] However, some of these methods have major limitations in their utility, including severe reaction conditions, reagent harmfulness and the need for metal-catalysts, complex ligands and additives.[9-12] Therefore, the development of viable synthetic methods, balancing metal-free and atom-economical approaches for the synthesis of substituted phenols are thus important, which might offer new avenues for the assembly of carbo/heterocycles.



Scheme 1: Metal-free insertion of alkynes into C-C σ-bond

Results and discussion

As part of our ongoing work on 2-alkynyl arylaldehydes and their derivatives,[13] the reaction of 2-alkynyl indole-3-carbaldehyde **1a** with 1,3-diketone **2a** in the presence of NaOH has been carried out to produce the condensation product **A**. However, surprisingly the formation of 2,3,5-trisubstituted phenol **3a** was observed in 46% yield (Table 1,

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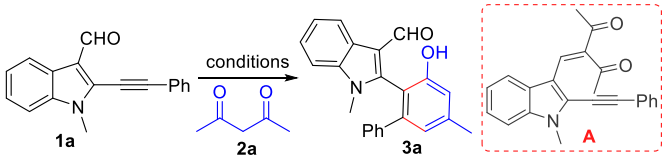
entry 1). Presumably, the phenol **3a** is the outcome of a domino alkyne insertion/intramolecular aldol reaction/ aromatization, a result which is also supported by the previous literature data. Furthermore, the structure of **3a** was confirmed by X-Ray analysis (Figure 1). This observation represents an insertion of a different type of alkyne (other than aryne/alkynone) in the presence of a base leading to a uniquely substituted phenol, which motivated us to further explore the scope of the reaction. In this direction, our studies initiated with the optimization of the conditions using **1a** with **2a** as the model reaction, and the results are presented in Table 1. A screening of different bases revealed that Cs_2CO_3 is more effective in giving 63% of **3a**, while others such as ^{t}BuOK, KOAc and K_2CO_3 offered low yields (Table 1, entries 2 to 5). Next, a range of solvents such as dimethyl sulfoxide, acetonitrile, 1,2-dichloroethane, toluene were screened to examine their effect on this reaction and it was found that they provided inferior yields (Table 1, entries 6 to 9) compared to the reaction in DMF. Upon changing the quantity of Cs_2CO_3 from 1 equivalent to 1.5 equivalent, the desired **3a** was obtained in 74% yield (Table 1, entry 10). Additional increase of base to 2 equivalents didn't improve the reaction outcome (Table 1, entry 11). We were pleased to find that the reaction at 120 °C gave **3a** in 85% yield (Table 1, entry 12). Either by increasing the temperature to 140 °C or the reaction time to 15 hours, no further enhancement in the result was observed (Table 1, entry 13 & 14). No reaction ensued in the absence of the base (Table 1, entry 15), which shows that the base is necessary for the reaction.

Table 1: Optimisation of reaction conditions[a]



Entry	Base (equiv.)	Solvent	Temperature (°C)	Time (h)	Yield of **3a** (%)
1	NaOH (1)	DMF	100	8	46
2	^{t}BuOK (1)	DMF	100	10	19
3	KOAc (1)	DMF	100	12	trace
4	Cs_2CO_3 (1)	DMF	100	12	63
5	K_2CO_3 (1)	DMF	100	12	49
6	Cs_2CO_3 (1)	DMSO	100	8	52
7	Cs_2CO_3 (1)	CH_3CN	100	10	32
8	Cs_2CO_3 (1)	1,2-DCE	100	12	19
9	Cs_2CO_3 (1)	toluene	100	14	7
10	Cs_2CO_3 (1.5)	DMF	100	12	74
11	Cs_2CO_3 (2)	DMF	100	12	75
12	**Cs_2CO_3 (1.5)**	**DMF**	**120**	**11**	**85**
13	Cs_2CO_3 (1.5)	DMF	140	11	85
14	Cs_2CO_3 (1.5)	DMF	120	15	85
15	-	DMF	120	15	NR

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol) in 3 mL of solvent was stirred for given time; [b]Isolated yield; NR = no reaction

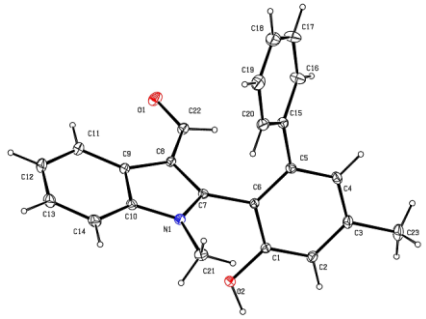
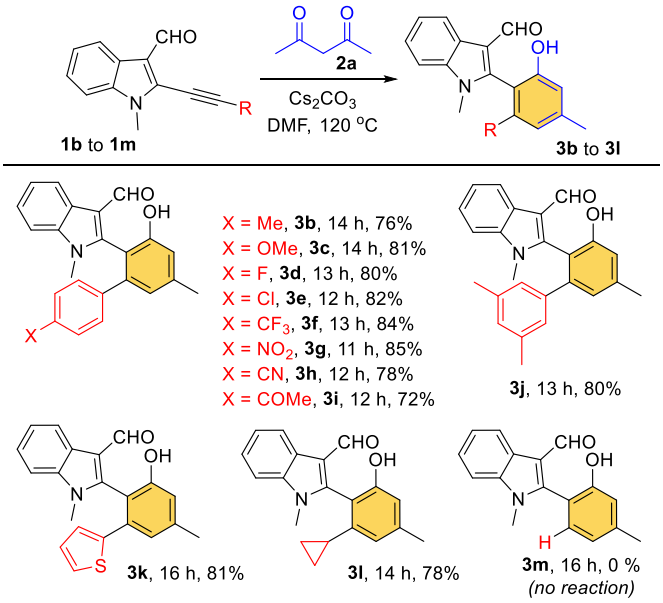


Figure 1: Crystal Structure of **3a (**CCDC No. 2217042**)**

Therefore, the conditions described in entry 12 were found to be optimal for this domino alkyne insertion /intramolecular aldol reaction/aromatization. Having the optimized reaction conditions, the feasibility of the present transformation with a variety of 2-indolyl alkynes tethered with electronically divergent substitutions was studied and the results are summarized in Table 2. Initially, alkynes bearing electron-donating aryl groups such as *p*-methylphenyl (**1b**) and *p*-methoxyphenyl (**1c**) reacted smoothly with **2a** to provide the desired phenols **3b** and **3c** in 76% and 81% of yields, respectively. Likewise, when alkynes with electron-withdrawing aryl groups such as 4-fluorophenyl, 4-chlorophenyl, 4-trifluoromethylphenyl, 4-nitrophenyl, 4-cyanophenyl and 4-acetylphenyl (**1d** to **1i**) were treated with 1,3-diketone **2a**, the reaction progressed efficiently to offer the corresponding 2-indolyl phenols **3d** to **3i** in good yields. The alkynes holding 3,5-dimethylphenyl (**1j**), 2-thiophenyl (**1k**, heteroaryl) groups were also successfully employed to react with **2a** giving the target products **3j** and **3k** in 80% and 81% yields, respectively.

Table-2 Substrate scope[a]



Reaction conditions: A mixture of **1** (0.3 mmol) and **2a** (0.3 mmol) in the presence of Cs_2CO_3 (1.5 equiv.) in 3 mL of DMF was stirred at 120 °C for the given time; All the yields given are isolated yields.

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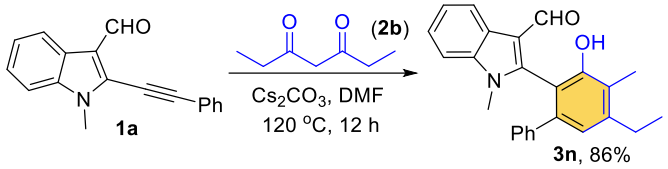
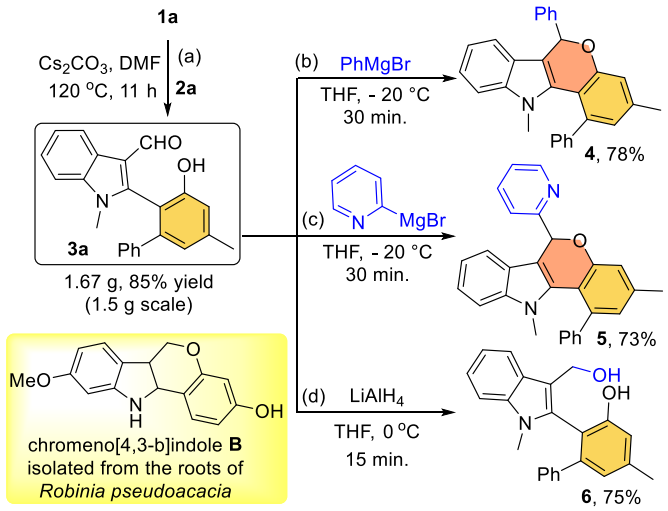
Agreeably, altering the substituent on the indolyl-alkyne from aryl to alkyl group (cyclopropyl, **1l**) was found to be suitable to obtain the phenol **3l** in 78% yield. However, unsubstituted-alkynyl indole **1m** failed to participate in the reaction. All these compounds have spectra and analytical data in agreement with the proposed structures.

Gratifyingly, diverse alkyl substitutions could be effectively introduced on the phenol by employing the reaction of **1a** with a different 1,3-dialkylketone, heptane-3,5-dione (**2b**) to obtain the 2,3,5,6-tetrasubstituted phenol **3n** in 86% yield *via* domino alkyne insertion/intramolecular aldol reaction/aromatization (Scheme 2).



Scheme 2: Reactions of heptane-3,5-dione with **1a**

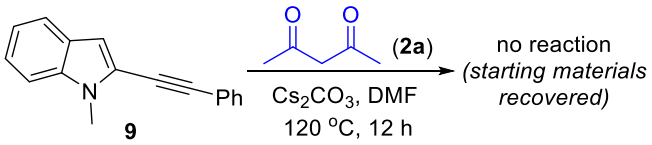
To confirm that the developed domino reaction is scalable, 1.5 g of the 2-indolyl alkyne **1a** was treated with pentane-2,4-dione (**2a**) under the optimal conditions to give **3a** (1.67 g) in 85% yield (Scheme 3a). To highlight the synthetic utility of the 2-indolyl phenols obtained above, next we embarked on the synthesis of chromeno-indoles, a key framework of pharmaceutically important molecules and natural products, such as **B** (Scheme 3).[14] Taking the advantage of aldehyde and phenolic hydroxyl functionalities in **3a**, a novel approach was developed to access dihydrochromeno-indoles by the treatment of **3a** with phenylmagnesium bromide, which delivered the dihydrochromeno[4,3-b]indole **4** in 78 % yield (Scheme 3b). Similarly, the reaction of **3a** with 2-pyridylmagnesium bromide, was also effective to afford the dihydrochromeno[4, 3-b]indole **5** in 73% yield (Scheme 3c).



Scheme 3 Transformations of **3a** to chromeno-indoles and **6**

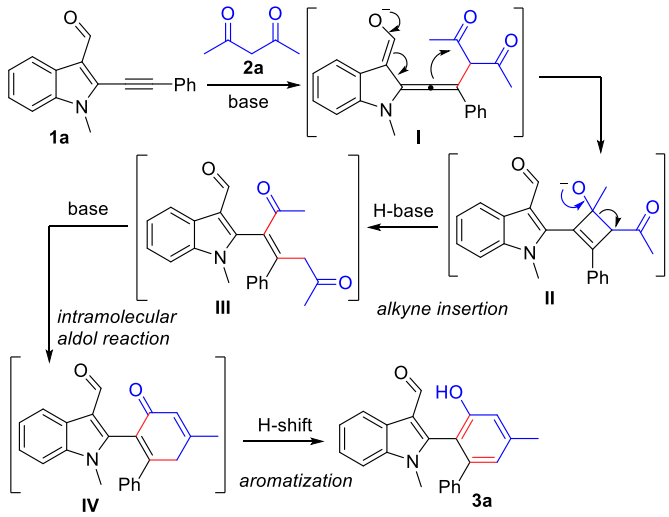
In addition, the reduction of aldehyde in **3a** using lithium aluminium hydride was also fruitful to provide the alcohol **6** in 75% yield (Scheme 3d).

To understand the role of aldehyde group in alkyne and to gain insight into the reaction mechanism, a control experiment was conducted (Scheme 4). The reaction of 2-alkynyl indole **9**[15] with 1,3-dikotene **2a** under the standard reaction conditions, failed to proceed for alkyne insertion. This result indicates that the aldehyde is facilitating the alkyne insertion.



Scheme 4: Control experiment

Based on previous results and literature data,[6a] a plausible reaction mechanism is proposed in Scheme 5. Initially, addition of the 1,3-diketone **2a** to 2-alkynyl indole **1a** under basic conditions provides an intermediate **I**. An intramolecular C-nucleophilic addition of **I** delivers a strained intermediate **II**, which subsequently undergoes C-C bond cleavage which leads to alkyne insertion (acylative alkylation of the alkyne) intermediate **III**. Next, an intramolecular aldol condensation to cross conjugated cyclohexadienone **IV,** followed by H-shift (aromatization), affords the phenol **3a.**



Scheme 5: Plausible reaction mechanism

Conclusions

In summary, we have established a protocol for the synthesis of diversely substituted 2-indolyl phenols through a base-mediated reaction of indolyl 2-alkynes with 1,3-diketones in a single step. The reaction proceeds through the insertion of indole-tethered alkyne into a C-C single bond of a 1,3-diketone followed by intramolecular aldol reaction/aromatization. This protocol offers an elegant

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unique strategy to dihydrochromeno[4, 3-b]indoles, demonstrating the synthetic applicability. Overall, the method showed advantages such as metal-free conditions, easy to scale up and the products are suitable for further transformations.

Experimental section

General Information: All the reactions were performed in oven-dried reaction vial with magnetic stirring bar under closed condition and air and moisture sensitive reactions were performed under inert atmosphere (nitrogen) using reagent grade solvents. Commercially available reagents/ starting material **2** and **4** were used as such without any further purification. All reactions were monitored by thin-layer chromatography carried out on silica plates using UV-light, anisaldehyde and *β*- naphthol for visualization. Column chromatography was performed on silica gel (100–200 mesh) using hexanes and ethyl acetate as eluent. ^{1}H NMR was recorded in $CDCl_3$ and DMSO-D_6 on 500 MHz and 400 MHz instruments and ^{13}C NMR was recorded on 75 MHz, 101 MHz, and 126 MHz. *δ* 7.26 and δ 77 are corresponding to $CDCl_3$ and *δ* 2.5 and δ 39.52 corresponding to DMSO-D_6 in ^{1}H NMR and ^{13}C NMR respectively, *δ* 1.56 and *δ* 3.30 related to moisture present in $CDCl_3$ and DMSO-D_6, respectively. *δ* 8.32 and δ 79.16 peaks orresponding to $CHCl_3$ traces observed in ^{1}H NMR and ^{13}C NMR in DMSO-D_6, respectively. Chemical shifts were reported in *δ* (ppm) relative to TMS as an internal standard and *J* values were given in Hz (hertz). Multiplicity is indicated as, *s* (singlet); *d* (doublet); *t* (triplet); *m* (multiplet); dd (doublet of doublets), td (triplet of doublet) etc. FT-IR spectra were recorded on Alpha (Bruker) infrared Spectrophotometer. High-resolution mass spectroscopy (HRMS) [ESI+] were obtained using either a TOF or a double-focusing spectrometer.

1-Methyl-2-(arylethynyl)-1H-indole-3-carbaldehyde (**1**) were Prepa red using the reported procedure and spectral data was compared (**1a**, **1b**, **1c**, **1f**, **1l**, **1m**)[16] and (**1g**).[17] Analytical data for **1d**, **1e**, **1h**, **1i**, **1j** and **1k** provided herewith.

General Procedure (A) for the preparation of 1-methyl-2-(arylethynyl)-1H-indole-3-carbaldehyde (1)

To the solution of 2-ethynyl-1-methyl-1H-indole-3-carboxaldehyde (1.0 equiv) and aryl iodide (1.05 equiv) was added to triethylamine (10 vol.) and THF (10 vol.) and purged with nitrogen for 15 min. $Pd(PPh_3)_2Cl_2$ (3 mol%) and CuI (1.5 mol%) were added and stirred at room temperature for 5 h. The reaction mixture was filtered and washed by EtOAc (5 vol.). The filtrate was washed by water (5 vol. x 2), and brine (5 vol.) , organic layer dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate in hexanes) to obtain 1-methyl-2-(arylethynyl)-1H-indole-3-carbaldehyde (1).

2-((4-Fluorophenyl) ethynyl)-1-methyl-1H-indole-3-carbaldehyde (1d)

Following the general procedure **A**, 2-ethynyl-1-methyl-1H-indole-3-carboxaldehyde((183 mg, 1.0 mmol) allowed to react with 1-iodo-4-fluoro benzene (233 mg, 1.05 mmol)in 1.83 mL TEA, and 1.83 mL THF for 5 h. After the work-up, the residue was purified by column chromatography on silica gel (10 % Ethyl acetate in hexanes) to afford **1d** (202.94 mg, 73 %), as white solid; *Rf* = 0.85 (*n*-hexane: Ethyl acetate = 8:2) mp.:135–139 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.35 – 8.32 (m, 1H), 7.64 – 7.60 (m, 2H), 7.42 – 7.32 (m, 3H), 7.16 – 7.11 (m, 2H), 3.93 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 185.1, 164.7, 162.2, 137.6, 134.0, 133.9, 131.8, 125.2, 124.5, 123.6, 122.2, 119.9, 117.5, 116.3, 116.1, 109.7, 100.1, 31.3; IR (KBr): 3439, , 2931, 1649, 1598, 1466, 1384, 1333, 1226, 1043, 744 cm^{-1}; m/z (ESI): [M + H]$^+$278.00; HRMS (ESI): *m/z* calcd for $C_{18}H_{13}FNO$ [M + H] $^+$: 278.0976, found: 278.0968.

2-((4-Chlorophenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (1e)

Following the general procedure **A**, 2-ethynyl-1-methyl-1H-indole-3-carboxaldehyde (183 mg, 1.0 mmol) allowed to react with 1-iodo-4-chloro benzene (249 mg, 1.05 mmol) in 1.83 mL TEA, and 1.83 mL THF for 5 h. After the work-up, the residue was purified by column chromatography on silica gel (10 % Ethyl acetate in hexanes) to afford **1e** (219.75 mg, 75 %) as white solid; *Rf* = 0.8 (*n*-hexane: Ethyl acetate = 8:2) mp.:160 –162 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 10.27 (s, 1H), 8.35 – 8.32 (m, 1H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.43 – 7.38 (m, 3H), 7.37 – 7.32 (m, 2H), 3.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 185.1, 137.6, 136.1, 133.1(2C), 131.5, 129.2(2C), 125.2, 124.5, 123.7, 122.3, 120.1, 119.8, 109.8, 99.9, 78.5, 31.3; IR (KBr): 3305, 2843, 2163, 1643, 1466, 1402, 1212, 1110, 1017, 713 cm^{-1}; m/z (ESI): [M + H]$^+$ 293.95; HRMS (ESI): *m/z* calcd for $C_{18}H_{13}ClNO$ [M + Na] $^+$ 316.0499, found 316.0507.

4-((3-Formyl-1-methyl-1H-indol-2-yl)ethynyl)benzonitrile(1h)

Following the general procedure **A**, 2-ethynyl-1-methyl-1H-indole-3-carboxaldehyde (183 mg, 1.0 mmol) allowed to react with 1-iodo- 4-iodobenzonitrile (240 mg, 1.05 mmol) in 1.83 mL TEA, and 1.83 mL THF for 5 h. After the work-up, the residue was purified by column chromatography on silica gel (10 % Ethyl acetate in hexanes) to afford **1h** (213.75 mg, 75 %) as white solid; *Rf* = 0.8 (*n*-hexane: Ethyl acetate = 8:2); mp.:165 – 168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 10.28 (s, 1H), 8.34 (d, *J* = 7.7 Hz, 1H), 7.72 (s, 4H), 7.45 – 7.34 (m, 3H), 3.95 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 184.8, 137.8, 132.4 (2C), 132.3 (2C), 130.3, 126.1, 125.7, 124.5, 123.9, 122.4, 120.8, 118.1, 113.1, 109.9, 98.9, 81.5, 31.4; IR (KBr): 3058, 2229, 1657, 1605, 1386, 1130, 1046, 844; m/z (ESI): [M + H]+ 285.05; HRMS (ESI): *m/z* calcd for $C_{19}H_{13}N_2O$ [M + H] $^+$: 285.1023, found 285.1026.

2-((4-Acetylphenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (1i)

Following the general procedure **A**, 2-ethynyl-1-methyl-1H-indole-3-carboxaldehyde(183 mg, 1.0 mmol) allowed to react with 1-(4-iodophenyl)ethan-1-one (258 mg, 1.05 mmol) in 1.83 mL TEA, and 1.83 mL THF for 5 h. After the work-up, the residue was purified by column chromatography on silica gel (10 % Ethyl acetate in hexanes) to afford **1i** (205.36 mg, 68 %), as white solid; *Rf* = 0.5 (*n*-hexane: Ethyl acetate = 8:2), mp.:170–178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 10.26 (s, 1H), 8.32 – 8.30 (m, 1H), 7.98 (d, *J* = 8.3 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.40 – 7.31 (m, 3H), 3.90 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 197.1, 184.9, 137.7, 137.4, 131.9 (2C), 131.0, 128.5 (2C), 125.9, 125.4, 124.5, 123.8, 122.3, 120.5, 109.8, 100.1, 80.4, 31.3, 26.7; IR (KBr): 3734, 2933, 1682, 1465, 1393, 1263, 1048, 758 cm^{-1}; m/z (ESI): [M + H]$^+$ 302.00; HRMS (ESI): *m/z* calcd for $C_{20}H_{16}NO_2$ [M + H]$^+$: 302.1175, found 302.1165.

2-((3,5-dimethylphenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde(1j)

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Following the general procedure **A**, 2-ethynyl-1-methyl-1H-indole-3-carboxaldehyde (183 mg, 1.0 mmol) allowed to react with 1-iodo-3,5-dimethylbenzene (244 mg, 1.05 mmol) in 1.83 mL TEA, and 1.83 mL THF for 5 h. After the work-up, the residue was purified by column chromatography on silica gel (10 % Ethyl acetate in hexanes) to afford **1j** (202 mg, 70%) as white solid; *Rf* = 0.7 (*n*-hexane: Ethyl acetate = 8:2); mp.:165–167 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.34 – 8.32 (m, 1H), 7.40 – 7.31 (m, 3H), 7.26 (s, 2H), 7.08 (s, 1H), 3.92 (s, 3H), 2.36 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.3, 138.4, 137.5, 132.5, 131.9, 129.5 (2C), 125.0, 124.5, 123.5, 122.2, 120.9, 119.8, 109.7, 101.9, 76.8, 31.2, 21.2 (2C); IR (KBr): 3021, 2921, 2859, 2194, 1694, 1451, 1224, 1109, 702 cm^{-1}; m/z (ESI): [M + H]$^+$ 287.95; HRMS (ESI): *m/z* calcd. For $C_{20}H_{18}NO$ [M + H]$^+$ 288.1383, found 288.1377.

1-Methyl-2-(thiophen-2-ylethynyl)-1H-indole-3-carbaldehyde (1k)

Following the general procedure **A**, 2-ethynyl-1-methyl-1H-indole-3-carboxaldehyde (183 mg, 1.0 mmol) allowed to react with 2-iodothiophene (219 mg, 1.05 mmol) in 1.83 mL TEA, and 1.83 mL THF for 5 h. After the work-up, the residue was purified by column chromatography on silica gel (10 % Ethyl acetate in hexanes) to afford **1k** (202 mg, 76 %), as white solid; *Rf* = 0.7 (*n*-hexane: Ethyl acetate = 8:2 mp.: mp.: 140–145 °C ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.34 – 8.32 (m, 1H), 7.46 – 7.44 (m, 2H), 7.41 – 7.32 (m, 3H), 7.10 (dd, J = 5.1, 3.7 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.1, 137.6, 133.9, 131.6, 129.5, 127.6, 125.2, 124.5, 123.6, 122.3, 121.0, 120.0, 109.7, 94.4, 81.2, 31.3; IR (KBr): 2929, 1650, 1464, 1404, 1223, 1040, 741; m/z (ESI): [M + H]$^+$ 266; HRMS (ESI): *m/z* calcd for $C_{16}H_{12}NOS$ [M + H]$^+$ 266.0640 found: 266.0634.

General Procedure B for preparation of 2-indolyl phenols (3)

To the solution of 1-Methyl-2-aryllethynyl-1H-indole-3-carbalde hyde (**1**) (0.3 mmol, 1.0 equiv) in DMF (3 mL) at room temperature. Cs_2CO_3 (0.45 mmol, 1.0 equiv) and pentane-2,4-dione (0.3 mmol, 1 equiv) was added and heated at 120 °C for 11 h under stirring 11 h to 16 h. The reaction mixture was diluted with water (10 mL) and extracted by EtOAc (10 mL x 2). The organic layers were combined, washed by water (10 mL x 2), and brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford substituted phenols (**3**)

2-(3-Hydroxy-5-methyl-[1,1'-biphenyl]-2-yl)-1-methyl-1H-indole-3-carbaldehyde (3a)

Following the general procedure **B**, 1-Methyl-2-phenylethynyl-1H-indole-3-carbaldehyde (**1a**) (78 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and pentane-2,4-dione (30 mg, 0.3 mmol) in DMF (3 ml) at 120 °C for 11 h to obtain **3a** (82 mg, 85 %) as a yellow solid. *Rf* = 0.3 (n-hexane: ethyl acetate = 8:2), mp.:168 – 170 °C, ^{1}H NMR (400 MHz, DMSO-D_6) δ 10.14 (s, 1H), 9.39 (s, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.62 – 7.60 (d, *J* = 8.1 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.27 – 7.18 (m, 4H), 7.12 – 7.09 (m, 2H), 6.97 (s, 1H), 6.90 (d, *J* = 0.7 Hz, 1H), 3.62 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (101 MHz, DMSO-D_6) δ 185.2, 157.0, 149.0, 144.7, 141.7, 140.1, 137.5, 128.7(2C), 128.6(2C), 127.6, 124.1, 123.4, 122.8, 122.2, 121.0, 115.8, 114.3, 111.5, 111.0, 30.1, 21.7. ; IR (KBr): 3346, 2945, 2838, 1651, 1456, 1113, 1019 cm^{-1}; m/z (ESI): [M + H]$^+$ 342.05; HRMS (ESI): *m/z* calcd for $C_{23}H_{20}NO_2$ [M + H] $^+$: 342.1494, found 342.1490.

2-(3-Hydroxy-5,4'-dimethyl-biphenyl-2-yl)-1-methyl-1H-indole-3-carbaldehyde (3b)

Following the general procedure **B**, 1-Methyl-2-p-tolylethynyl-1H-indole (**1b**) (82 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and Pentane-2,4-dione (30 mg, 0.3 mmol) in DMF (3 ml) at 120 °C (3 ml) for 14 h to obtain **3b** (81 mg, 76 %), yellow solid, *Rf* = 0.3(n-hexane: ethyl acetate = 8:2), mp.: 248 – 251 °C, ^{1}H NMR (400 MHz, DMSO-D_6) δ 10.03 (s, 1H), 9.33 (s, 1H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.28-7.24 (m, 1H), 7.20(t, *J* = 7.2 Hz, 1H), 6.97 – 6.92 (m, 4H), 6.89 (s, 1H), 6.81 (s, 1H), 3.56 (s, 3H), 2.38 (s, 3H), 2.16 (s, 3H); ^{13}C NMR(101 MHz, DMSO-D_6) δ 185.3, 157.0, 149.2, 144.6, 141.6, 138.1, 137.5, 136.7, 129.3(2C), 128.6(2C), 125.0, 123.4, 122.8, 122.2, 121.1, 115.6, 114.2, 111.4, 111.1, 30.1, 21.7, 21.0; IR (KBr): 3710, 3368, 2880, 2256, 1660, 996, 825, 765 cm^{-1}; m/z (ESI): [M + H]$^+$ 356.00; HRMS (ESI): *m/z* calcd for $C_{24}H_{22}NO_2$ [M + H]$^+$: 356.1651, found 356.1649.

2-(3-Hydroxy-4'-methoxy-5-methyl-biphenyl-2-yl)-1-methyl-1H-indole-3-carbaldehyde (3c)

Following the general procedure **B**, 2-(4-Methoxy-phenylethynyl)-1-methyl-1H-indole (**1c**) (86 mg, 0.3 mmol) was treated with Cs_2CO_3(147 mg, 0.45 mmol) and Pentane-2,4-dione (30 mg, 0.3 mmol) in DMF (3 ml) at 120 °C for 14 h to obtain **3c** (90 mg, 81 %), white solid, *Rf* = 0.25 (n-hexane: ethyl acetate = 8:2), mp.: 256-259 °C; ^{1}H NMR (500 MHz, DMSO-D_6) δ 10.00 (s, 1H), 9.33 (s, 1H), 7.98(d, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.28 – 7.18 (m, 2H),6.98-6.96 (m, 2H), 6.86 (s, 1H), 6.81 (s, 1H), 6.72-6.70 (d, *J* = 8.8 Hz, 2H), 3.63 (s, 3H), 3.55 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, DMSO-D_6) δ 184.8, 158.2, 156.5, 148.8, 143.8, 141.1, 137.1, 132.7, 129.4 (2C), 124.5, 122.9, 122.3, 121.7, 120.6, 114.8, 113.6, 113.5 (2C), 110.8, 110.6, 54.9, 30.4, 21.1; IR (KBr): 3816, 3327, 2946, 1647, 1455, 1019 cm^{-1}; m/z (ESI): [M + H]$^+$ 372.05; HRMS (ESI): *m/z* calcd for $C_{24}H_{22}NO_3$ [M + H]$^+$: 372.1600, found 372.1600.

2-(4'-Fluoro-3-hydroxy-5-methyl-biphenyl-2-yl)-1-methyl-1H-indole-3-carbaldehyde (3d)

Following the general procedure **B**, 2-(4-Fluoro-phenylethynyl)-1-methyl-1H-indole (**1d**) (83 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and pentane-2,4-dione (30 mg, 0.3 mmol) in DMF(3 ml) at 120 °C for 13 h to obtain **3d** (86 mg, 80 %), white solid, *Rf* =0.2 (n-hexane: ethyl acetate = 8:2), mp.: 245 – 247 °C ,^{1}H NMR (400 MHz, DMSO-D_6) δ 10.10 (s, 1H), 9.33 (s, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.22 – 7.18 (m, 1H), 7.10 – 7.06 (m, 2H), 7.01 – 6.97 (m, 2H), 6.91 (s, 1H), 6.84 (s, 1H), 3.56 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, DMSO-D_6) δ 185.2, 157.1, 148.7, 143.6, 141.8, 137.6, 137.4, 130.8 (2C), 130.7, 124.1, 123.5, 122.9, 122.2, 121.1, 115.9, 115.6, 115.4, 114.2, 111.5, 111.1, 31.0, 21.6; IR (KBr): 3852, 3699, 3110, 2881, 2681, 1726, 1630, 1229 cm^{-1}; m/z (ESI): [M + H]$^+$ 360.05; HRMS (ESI): *m/z* calcd for $C_{23}H_{19}FNO_2$ [M + H] $^+$: 360.1400, found 360.1394.

2-(4'-Chloro-3-hydroxy-5-methyl-biphenyl-2-yl)-1-methyl-1H-indole-3-carbaldehyde (3e)

Following the general procedure **B**, 2-(4-Chloro-phenylethynyl)-1-methyl-1H-indole (**1e**) (88 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and pentane-2,4-dione (30 mg, 0.3 mmol) in DMF(5 ml) at 120 °C for 12 h to obtain **3e** (92 mg, 82 %), white solid, *Rf* = 0.3 (n-hexane: ethyl acetate =8:2), mp.:250 – 255 °C, ^{1}H NMR (400 MHz, DMSO-D_6) δ 10.14 (s, 1H), 9.33 (s, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 8.1 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.24 – 7.19 (m, 3H), 7.09 – 7.06 (m, 2H), 6.93 (s, 1H), 6.85 (s, 1H), 3.58 (s, 3H), 2.39 (s, 3H); ^{13}C NMR. (101 MHz, DMSO-D_6) δ 185.2, 157.1, 148.6, 143.4, 141.9, 139.9, 137.6, 132.4, 130.6 (2C) , 128.7 (2C) , 124.1, 123.5,

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122.9, 122.1, 121.1, 116.1, 114.2, 111.4, 111.2, 31.0, 21.6; IR (KBr): 3852, 3205, 2881, 2791, 1726, 1381, 1229 cm^{-1}; m/z (ESI): $[M + H]^+$ 376.10; HRMS (ESI): *m/z* calcd for $C_{23}H_{19}ClNO_2$ $[M + H]^+$: 376.1104 , found 376.1102.

2-(3-Hydroxy-5-methyl-4'-trifluoromethyl-biphenyl-2-yl)-1-methyl-1H-indole-3-carbaldehyde (3f)

Following the general procedure **B**, 1-Methyl-2-(4-trifluoromethyl-phenylethynyl)-1H-indole (**1f**) (98 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and pentane-2,4-dione (30 mg, 0.3 mmol) in DMF(3 ml) at 120 °C for 13 h to obtain **3f** (103 mg, 84 %), yellow solid, *Rf* = 0.3(n-hexane: ethyl acetate = 8:2), mp.: 165 – 167 °C, ^1H NMR (400 MHz, DMSO-D_6) δ 10.19 (s, 1H), 9.32 (s, 1H), 8.32 (s, 1H), 7.96 (d, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.40 – 7.32 (m, 4H), 7.29 – 7.25 (m, 1H), 7.19 (t, *J* = 7.4 Hz, 1H), 6.96 (s, 1H), 6.93 (s, 1H) 3.58 (s, 3H), 2.41 (s, 3H) ; ^{13}C NMR (101 MHz, DMSO-D_6) δ 185.0, 157.2, 148.2, 142.9, 142.1, 141.8, 137.6, 132.8, 129.7, 125.2 (2C), 124.9, 124.3, 124.2, 123.6, 122.9, 122.1, 121.0, 116.5, 114.4, 111.6, 111.0, 30.9, 21.6; IR (KBr): 3860, 3744, 3631, 2931, 1637, 1464, 1051, 806 cm^{-1}; m/z (ESI): $[M + H]^+$ 410; HRMS (ESI): *m/z* calcd for $C_{24}H_{19}F_3NO_2$ $[M + H]^+$: 410.1368, found 410.1359.

2-(3-Hydroxy-5-methyl-4'-nitro-biphenyl-2-yl)-1-methyl-1H-indole-3-carbaldehyde (3g)

Following the general procedure **B**, 1-Methyl-2-(4-nitro-phenylethynyl)-1H-indole (**1g**) (91 mg, 0.3 mmol) was treated with Cs_2CO_3(147 mg, 0.45 mmol) and pentane-2,4-dione (30 mg, 0.3 mmol) in DMF(3 ml) at 120 °C for 11 h to obtain **3g** (99 mg,75 %), yellow solid, *Rf* = 0.15 (n-hexane: ethyl acetate = 8:2), mp.:148 – 150 °C, ^1H NMR (300 MHz, DMSO-D_6) δ 10.30 (s, 1H), 9.31 (s, 1H), 8.02 (d, *J* = 8.7 Hz, 2H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 2H), 7.29 – 7.18 (m, 2H), 6.99(s, 2H), 3.63 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, DMSO-D_6) δ 185.0, 157.3, 147.1, 147.9, 146.8, 142.6, 142.2, 137.6 , 130.2(2C), 124.9, 123.8(2C), 123.7, 123.0, 122.1, 121.1, 116.1, 114.4, 111.4, 111.3, 31.1, 21.6.; IR (KBr): 3385, 2929, 1632, 1339, 1021, 747cm^{-1}; m/z (ESI): $[M + H]^+$ 387.05; HRMS (ESI): *m/z* calcd for $C_{23}H_{19}N_2O_4$ $[M + H]^+$: 387.1345, found 387.1345.

2'-(3-Formyl-1-methyl-1H-indol-2-yl)-3'-hydroxy-5'-methyl-biphenyl-4-carbonitrile (3h)

Following the general procedure **B**, 4-(1-Methyl-1H-indol-2-ylethynyl)-benzonitrile (**1h**) (85 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and pentane-2, 4-dione (30 mg, 0.3 mmol) in DMF (3 ml) at 120 °C for 12 h to obtain **3h** (86 mg, 78 %), yellow solid, *Rf* = 0.2 (n-hexane: ethyl acetate = 8:2), mp.: 260 – 262 °C, ^1H NMR (400 MHz, DMSO-D_6) δ 10.24 (s, 1H), 9.31 (s, 1H), 7.97 (d, *J* = 7.7 Hz, 1H), 7.64(d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.31 – 7.19 (m, 4H), 6.97 (s, 1H), 6.88 (s, 1H), 3.60 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, DMSO-D_6) δ 185.1, 157.2, 148.0, 145.8, 143.0, 142.2, 137.6, 132.6 (2C), 129.9 (2C) , 124.9, 123.6, 123.0, 122.1, 121.1, 119.0, 116.8, 114.3, 111.4, 111.2, 110.3, 31.1, 21.6 cm^{-1}; IR (KBr):3841, 3624, 3331, 2825, 2291, 1790, 1633, 1328, 1128; m/z (ESI): $[M + H]^+$ 367.00; HRMS (ESI): *m/z* calcd for $C_{24}H_{19}N_2O_2$ $[M + H]^+$: 367.1447, found 367.1448.

2-(4'-Acetyl-3-hydroxy-5-methyl-[1,1'-biphenyl]-2-yl)-1-methyl-1H-indole-3-carbaldehyde(3i)

Following the general procedure **B**, 2-((4-acetylphenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (**1i**) (90 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and pentane-2,4-dione (30 mg, 0.3 mmol) in DMF (3 ml) at 120 °C for 12 h to obtain **3i** (83 mg, 72 %), yellow solid, *Rf* = 0.2 (n-hexane: ethyl acetate = 8:2), mp.:175 – 180°C; ^1H NMR (500 MHz, DMSO-D_6) δ 10.09 (s, 1H), 9.24 (s, 1H), 8.28 – 8.27 (m, 1H), 7.95 (d, *J* = 7.7 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.28 – 7.25 (m, 1H), 7.20 – 7.16 (m, 2H), 7.11 – 7.09 (m, 1H), 7.04 (s, 1H), 6.96 (s, 1H), 3.61 (s, 3H), 3.32 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, DMSO-D_6) δ 201.3, 198.1, 147.8, 142.2, 142.1, 138.6, 135.7, 132.7, 131.2, 129.8(2C), 129.7, 128.6(2C), 127.3, 127.1, 122.7, 122.4, 121.3, 120.3, 111.9, 110.3, 30.4, 29.8, 27.3; IR (KBr): 3767, 3486, 2930, 1721, 1462, 1269, 1029, 635 cm^{-1}; m/z (ESI): $[M + H]^+$ 384.10; HRMS (ESI): *m/z* calcd for $C_{25}H_{22}NO_3$ $[M + H]^+$: 384.1594, found 384.1588.

2-(3-hydroxy-3',5,5'-trimethyl-[1,1'-biphenyl]-2-yl)-1-methyl-1H-indole-3-carbaldehyde(3j)

Following the general procedure **B**, 2-((3,5-dimethylphenyl) ethynyl)-1-methyl-1H-indole-3-carbaldehyde (**1j**) (86 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and pentane-2,4-dione (30 mg, 0.3 mmol) in DMF (3 ml) at 120 °C for 13 h to obtain **3j** (89 mg, 80 %), yellow solid, *Rf* =0.3 (n-hexane: ethyl acetate =8:2), mp.: 230 – 232 °C, ^1H NMR (400 MHz, DMSO-D_6) δ 10.02 (s, 1H), 9.32 (s, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.22 – 7.18 (m, 1H), 6.88 (s, 1H), 6.83 (s, 1H), 6.74 (s, 1H), 6.62 (s, 2H), 3.54 (s, 3H), 2.38 (s, 3H), 2.01 (s, 6H); ^{13}C NMR (126 MHz, DMSO-D_6) δ 185.2, 156.9, 149.3, 144.8, 141.6, 140.8, 137.5, 137.3 (2C), 128.9, 126.5 (2C), 124.9, 123.4, 122.8, 122.0, 121.0, 115.6, 114.5, 111.4, 110.9, 30.9, 21.7, 21.2 (2C); IR (KBr): 2920, 2852, 1609, 1460, 1369, 846, 748 cm^{-1}; m/z (ESI): $[M + H]^+$ 370.10; HRMS (ESI): *m/z* calcd for $C_{25}H_{24}NO_2$ $[M + H]^+$: 370.1807, found 370.1802.

2-(2-hydroxy-4-methyl-6-(thiophen-2-yl)phenyl)-1-methyl-1H-indole-3-carbaldehyde (3k)

Following the general procedure **B**, 1-methyl-2-(thiophen-2-ylethynyl)-1H-indole-3-carbaldehyde (**1k**) (79 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and Pentane-2,4-dione (30 mg, 0.3 mmol) in DMF (3 ml) at 120 °C for 16 h to obtain **3k** (84 mg, 81 %), yellow solid, *Rf* = 0.25(n-hexane: ethyl acetate = 8:2), mp.: 210-212 °C, ^1H NMR (500 MHz, DMSO-D_6) δ 10.09 (s, 1H), 9.39 (s, 1H), 8.07 (d, J = 7.7 Hz, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.36 (dd, J = 5.0, 1.1 Hz, 1H), 7.33 – 7.30 (m, 1H), 7.27 – 7.24 (m, 1H), 7.07 (s, 1H), 6.88 (s, 1H), 6.88 – 6.84 (m, 2H), 3.49 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, DMSO-D_6) δ 184.9, 157.4, 148.5, 142.0(2C) 137.7, 136.7, 127.8, 127.7, 126.5, 125.2, 123.7, 123.0, 121.5, 121.3, 116.0, 115.2, 111.3, 110.9, 30.7, 21.6; IR (KBr): 3113, 2824, 1628, 1470, 1378, 756 cm^{-1}; m/z (ESI): $[M + H]^+$ 348.05; HRMS (ESI): *m/z* calcd for $C_{21}H_{18}NO_2S$ $[M + H]^+$: 348.1058, found 348.1049.

3-Cyclopropyl-5-methyl-2-(1-methyl-1H-indol-2-yl)-phenol (3l)

Following the general procedure **B**, 2-Cyclopropylethynyl-1-methyl-1H-indole (**1l**) (67 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and pentane-2,4-dione (30 mg, 0.3 mmol) in DMF (3 ml) at 120 °C for 14 h to obtain **3l** (68 mg, 78 %), white solid, *Rf* = 0.4 (n-hexane: ethyl acetate = 8:2), mp.:205 – 208 °C, ^1H NMR (300 MHz, DMSO-D_6) δ 9.77 (s, 1H), 9.48 (s, 1H), 8.15 (d, J = 6.9 Hz, 1H), 7.63 (d, J = 7.5 Hz, 1H), 7.35 – 7.26 (m, 2H), 6.66 (s, 1H), 6.33 (s, 1H), 3.55 (s, 3H), 2.28 (s, 3H), 1.39 – 1.31 (m, 1H), 0.73 – 0.60 (m, 4H); ^{13}C NMR (101 MHz, DMSO-D_6) δ 185.4, 156.5, 149.6, 145.2, 141.4, 137.8, 125.2, 123.5, 122.1, 121.1, 115.2, 115.1, 113.7, 112.9, 111.3, 30.8, 21.8, 13.7, 9.7, 9.3; IR (KBr): 3395, 2935, 2844, 1669, 1467, 1252, 1024 cm^{-1}; m/z (ESI): $[M + H]^+$ 306.05; HRMS (ESI): *m/z* calcd for $C_{20}H_{20}NO_2$ $[M + H]^+$: 306.1488, found 306.1494.

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2-(5-ethyl-3-hydroxy-4-methyl-[1,1'-biphenyl]-2-yl)-1-methyl-1H-indole-3-carbaldehyde (3n)

Following the general procedure **B**, 1-Methyl-2-phenylethynyl-1H-indole-3-carbaldehyde (**1a**) (78 mg, 0.3 mmol) was treated with Cs_2CO_3 (147 mg, 0.45 mmol) and heptane-3,5-dione (**2b**) (38 mg, 0.3 mmol) in DMF (3 ml) at 120 °C for 15 h to obtain **3n** (95 mg, 86 %) as a yellow solid. Rf =0.3 (n-hexane: ethyl acetate = 8:2), mp.:165 – 167 °C, ^{1}H NMR (400 MHz, DMSO-D_6) δ 9.35 (s, 1H), 8.76 (s, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.29 – 7.19 (m, 2H), 7.13 (d, *J* = 6.8 Hz, 3H), 7.03 (d, *J* = 7.3 Hz, 2H), 6.91 (s, 1H), 3.52 (s, 3H), 2.73 (q, *J* = 7.5 Hz, 2H), 2.26 (s, 3H), 1.25 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-D_6) δ 184.7, 154.0, 148.7, 145.4, 140.9, 140.7, 137.2, 128.2(2C), 128.1(2C), 126.8, 124.6, 122.9(2C), 122.3, 121.3, 120.6, 114.2, 112.6, 110.6, 30.5, 26.3, 14.3, 11.8; IR (KBr): 3299, 2919, 1734, 1637, 1463, 1377, 1063 cm^{-1}; m/z (ESI): [M + H]$^+$ 370.00; HRMS (ESI): *m/z* calcd for $C_{25}H_{24}NO_2$ [M + H]$^+$: 370.1802, found 370.1806.

3, 11-Dimethyl-1, 6-diphenyl-6, 11-dihydrochromeno [4, 3-b] indole (4)

To a solution of 2-(3-hydroxy-biphenyl-2-yl)-1-methyl-1H-indole-3-carbaldehyde (**3a**) (170 mg, 0.5 mmol) in dry THF (10 mL) was added PhMgBr (1.1 mL, 1.1 mmol, 1 M in THF) dropwise at – 20 °C. The reaction was stirred for 30 min. The reaction mixture was diluted with water (10 mL) and extracted with diethyl ether (10 mL x3). The organic layers were combined and washed with brine (10 mL) and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure at the temperature 25 °C. The residue was purified by column chromatography on silica gel to afford **4** (156 mg,78 %), off white solid, *Rf* = 0.45 (n-hexane: ethyl acetate = 8:2), mp.:110 – 113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (*d*, *J* = 4.2 Hz, 1H), 7.22 (*t*, *J* = 6.8 Hz, 3H), 7.18 – 7.10 (m, 6H), 7.09 – 7.05 (m, 3H), 6.93 – 6.90 (m, 3H), 5.89 (s, 1H), 3.21 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8, 141.2, 138.8, 138.6, 138.2, 136.2, 131.9, 127.9 (2C), 127.8 (2C), 127.4 (3C), 127.1 (2C), 126.2, 124.4, 123.9, 120.6, 118.9, 117.4, 116.6, 113.1, 110.5, 108.9, 76.7, 31.5, 20.4;. IR (KBr): 3376, 3050, 1614, 1464, 986, 759; m/z (ESI): [M + H]$^+$: 402.25; HRMS (ESI): *m/z* calcd for $C_{29}H_{24}NO$ [M+H]$^+$= 402.1852, found: 402.1847.

3, 11-Dimethyl-1-phenyl-6-(pyridin-2-yl)-6, 11-dihydrochromeno [4, 3-b] indole (5)

To a solution of 2-(3-hydroxy-biphenyl-2-yl)-1-methyl-1H-indole-3-carbaldehyde (**3a**) (170 mg, 0.5 mmol) in dry THF (10 mL) was added 2-Pyridyl Magnesium Bromide (4.4 mL, 1.1 mmol, 0.25 M in 2-Me-THF) dropwise at – 20 °C. The reaction was stirred until completion and then quenched by addition of water. The aqueous layer was then extracted with diethyl Ether (10 mL x 3). The organic layers were combined and washed with brine (10 mL) and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure at the temperature 0-5 °C to obtain **5**, white solid, mp.:130 – 132 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.7 Hz, 1H), 7.42 (td, *J* = 7.7, 1.7 Hz, 1H), 7.21 – 7.15 (m, 7H), 7.13 – 7.09 (m, 1H), 6.93 (d, *J* = 5.6 Hz, 2H), 6.84 (dd, *J* = 11.1, 3.9 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.38 (d, *J* = 7.9 Hz, 1H), 5.76 (s, 1H), 3.31 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1, 156.1, 147.4, 143.8, 141.3, 141.2, 137.8, 136.8, 134.7, 128.8 (2C), 128.3 (2C), 126.9, 125.3, 123.2, 122.4, 121.7, 121.6, 119.6, 119.5, 117.1, 115.0, 113.5, 109.6, 68.4, 30.2, 21.5; IR (KBr): 3095, 3229, 3094, 2929, 1614, 1468, 763; m/z (ESI): [M + H]$^+$: 403.25; HRMS (ESI): *m/z* calcd for $C_{28}H_{23}N_2O$ [M+H]$^+$ = 403.1805, found 403.1802.

2-(3-(Hydroxymethyl)-1-methyl-1H-indol-2-yl)-5-methyl-[1,1'-biphenyl]-3-ol (6)

To a solution of 2-(3-hydroxy-biphenyl-2-yl)-1-methyl-1H-indole-3-carbaldehyde (**3a**) (170 mg, 0.5 mmol) in dry THF (10 mL) and cooled to 0 °C. Lithium aluminium hydride (28 mg, 0.75 mmol) was added and stirred for 15 min. The reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (10 mL x 2). The organic layers were combined and washed with brine (10 mL) and dried over Na_2SO_4, and concentrated under reduced pressure at the temperature 45 °C. The residue was purified by column chromatography on silica gel to afford **6** (122 mg,75 %), white solid, *Rf* = 0.45 (n-hexane: ethyl acetate = 8:2), mp.:140 – 142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.67 (m, 1H), 7.22 – 7.14 (m, 3H), 7.12 – 7.07 (m, 5H), 6.94 – 6.91 (m, 2H), 4.77 (d, *J* = 11.9 Hz, 1H), 4.65 (d, *J* = 11.9 Hzac st, 1H), 3.18 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.3, 143.7, 141.3, 140.6, 137.5, 132.7, 128.6 (2C), 128.2 (2C), 127.1, 126.9, 123.3, 122.2, 119.9, 118.7, 116.3, 114.1, 113.1, 109.7, 56.4, 30.2, 21.5; IR (KBr): 3458, 3052, 2929, 1567, 1464, 1339, 756 cm^{-1}; m/z (ESI): [M + Na]$^+$ 366.00; HRMS (ESI): *m/z* calcd for $C_{23}H_{21}NO_2$ [M + H] $^+$: 366.1464, found 366.1467.

Conflicts of interest

"There are no conflicts to declare".

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