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Metal-free propargylation/aza-annulation approach to substituted β-carbolines and evaluation of their photophysical properties†‡

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An efficient acid-catalyzed propargylation/aza-annulation sequence was developed under metal-free reaction conditions, thus leading to a one-pot synthesis of a variety of substituted β-carbolines starting from propargylic alcohols and indole 2-carbonyls. This versatile strategy was further extended to the synthesis of 5-azaindoles and 5-azabenzothiazoles. Optical properties suggested that manipulation of electron donor and acceptor moieties on β-carbolines has an impact on their ground and excited state electronic behavior. This leads to blue or green emission and should facilitate the development of organic light emitting diodes (OLEDs). Electrochemical and stability studies revealed that **4a-6** shows ease of redox activity and photostability during illumination.

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Introduction

Aza-heterocycles are an important and attractive class of molecules for both medicinal and materials chemistry.[1] β-Carbolines, composed of a pyridine conjugated with an indole unit (pyrido[3,4-*b*]indoles), as a family of aza-heterocycles, are privileged scaffolds in medicinal chemistry since they are the core of many molecules with potent biological and therapeutic activities.[2] Meanwhile, they are also essential frameworks of a variety of bio-active natural products such as Harman, Bauerine A, Eudistomin A, and Plakortamine A (Fig. 1).[3] β-Carbolines serve as valuable intermediates towards the synthesis of other novel heterocycles or natural products.[4] Recently, PyID-BTM (Fig. 1) based β-carbolines have been reported with remarkable photoluminescence quantum yields and red emission upon replacing the carbazole moiety.[5]

Thus, β-carbolines exhibit the electron deficient characteristic of the pyridine moiety which facilitates the balance of holes and electrons thereby enhancing the quantum efficiency of organic light-emitting diodes (OLEDs). In addition, β-carbolines with weak electron donating nature can be employed as electron transport materials in perovskite solar cell applications. Nonetheless, the studies on the photophysical properties of carboline derivatives are very limited and extensive investigations are required to extend their applications in organic electronics.[6]

In this context, the synthesis of β-carbolines substituted with various electron donor and acceptor units has attracted much attention from synthetic chemists. Besides the conventional Pictet–Spengler,[7] Bischler–Napieralski[8] and Graebe–Ullmann reactions,[9] a number of impressive methods have been developed towards the synthesis of β-carboline derivatives.[10–14] Among these approaches, alkyne-assisted cyclizations of functionalized indoles have emerged as signifi-

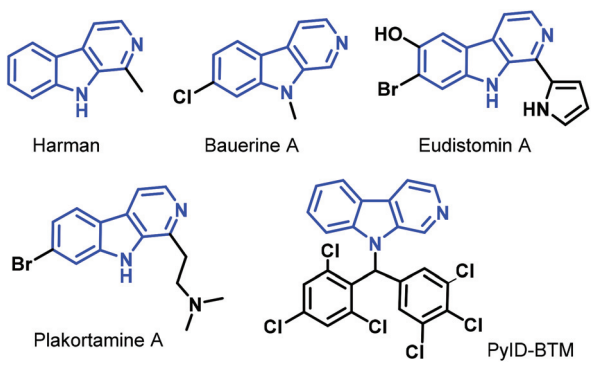

Fig. 1 Representative molecules with the β-carboline framework.

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‡ Electronic supplementary information (ESI) available: Copies of ^{1}H & ^{13}C NMR spectra of all new compounds and theoretical DFT calculations. See DOI: 10.1039/c9ob01959f

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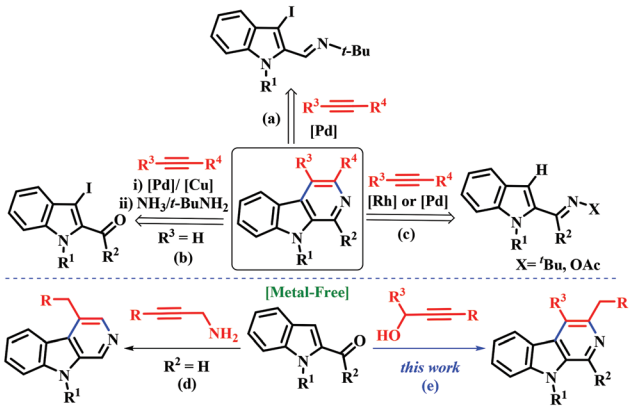


Scheme 1 Representative methods for the synthesis of β-carbolines from 2-carbonyl indoles and alkynes.

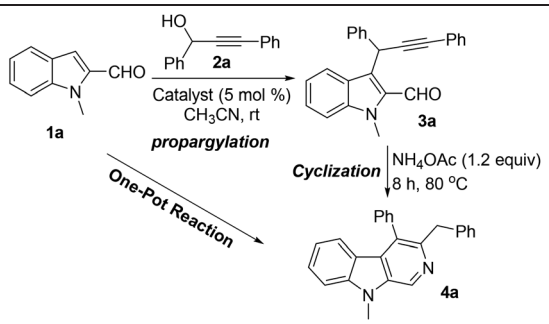
cant methods. For instance, Larock and co-workers have reported the palladium-catalyzed iminoannulation of acetylenes with *tert*-butylimines of halo-indolecarbonyls, which was further extended by others (Scheme 1a).[12] In addition, palladium/copper-catalyzed coupling and subsequent copper-catalyzed or thermal cyclization of terminal acetylenes have also been developed (Scheme 1b).[13] Later, C–H activation based synthetic methods involving indoloyl-ketone *O*-acetyl oximes or *tert*-butylimines of halo-indolecarbonyls and internal alkynes were also developed in the presence of metal-catalysts such as Rh and Pd (Scheme 1c).[14] Although elegant, these methods required the use of toxic and/or expensive transition metals towards alkyne-based annulations. Thus, the development of mild and metal-free reaction conditions for the synthesis of β-carbolines from indole-carbonyls should be of significant interest. In this direction, very recently base-mediated reaction of indole-carboxaldehyde with propargyl amines has been reported to access β-carbolines (Scheme 1d).[10i]

On the other hand, propargylic alcohols have received extensive attention as versatile synthons in the synthesis of various aromatic compounds and heterocycles, due to their easy accessibility as well as efficacy in direct nucleophilic reactions under mild reaction conditions.[15] We have successfully demonstrated the synthetic utility of 1-aryl propargylic alcohols in the preparation of various heterocyclic compounds such as furans, carbazoles, indoles, benzothiazoles and polyaromatic hydrocarbons.[16] As part of our long standing interest in utilizing propargylic alcohols, we sought a new synthetic possibility for rapid access to β-carbolines. Herein, we report a facile and metal-free synthesis of diversely substituted β-carbolines from the reaction of propargylic alcohols with indole 2-carbonyl compounds involving one-pot sequential propargylation/aza-annulations (Scheme 1e). The substitution pattern of the obtained β-carbolines is entirely different in the case of propargylic alcohols when compared with the reaction with propargylic amines (Scheme 1d). To the best of our knowledge, the direct use of propargylic alcohols to access β-carbolines is unknown. Furthermore, we have evaluated the photophysical properties of these new molecules and found that tuning of the various electron-donor and acceptor groups on β-carbolines leads to blue or green emission and potentially promote the design of diverse efficient OLED devices.

Results and discussion

Our synthesis of β-carbolines relies on the formation of 3-propargylated indole 2-carbonyls in the presence of acid-catalysis and aza-annulation under ammonium acetate conditions. Optimal reaction conditions for propargylation and successive treatment with NH_4OAc to generate β-carbolines are reported in Table 1. Based on literature precedence[17] and our earlier results,[16c] we have initiated the investigation with the reaction of 2-formyl indole **1a** with 1,3-diphenylprop-2-yn-1-ol (**2a**). In the presence of $BF_3{\cdot}Et_2O$ (5 mol%) the reaction gave 3-propargylated 2-formyl indole **3a** in a promising 75% yield (Table 1, entry 1). To our delight, the use of *p*TSA (5 mol%) could provide **3a** in 91% yield (Table 1, entry 2). Other catalysts such as $FeCl_3$, $CuOTf_2$, $AuCl_3$, AgOTf, CSA, $In(OTf)_3$ and $Sc(OTf)_3$ gave 3-propargylated product **3a** in moderate to good yields (Table 1, entries 3–9). Next, the aza-annulation of **3a** was tested in the presence of NH_4OAc as a nitrogen source[18] and the desired product **4a** was obtained in 89% yield at 80 °C, while at room temperature there was no progress in the reaction. As our objective was a one-pot conversion of 2-formyl indole to β-carboline **4a** without the isolation of **3a**, the reaction of **1a** with **2a** was performed in a one-pot approach by the successive

Table 1 Optimization of reaction conditions



Entry	Propargylation (catalyst/time)	Cyclization	Product	Yield[a] (%)
1	$BF_3{\cdot}Et_2O$/30 min	—	**3a**	75
2	*p*TSA/60 min	—	**3a**	91
3	$FeCl_3$/10 min	—	**3a**	60
4	$Cu(OTf)_2$/20 min	—	**3a**	78
5	$AuCl_3$/5 min	—	**3a**	70
6	AgOTf/60 min	—	**3a**	65
7	CSA/60 min	—	**3a**	70
8	$In(OTf)_3$/30 min	—	**3a**	60
9	$Sc(OTf)_3$/30 min	—	**3a**	50
10[b]	—	NH_4OAc	**4a**	89
11	***p*TSA/60 min**	**NH_4OAc**	**4a**	**85**
12[c]	*p*TSA/60 min	NH_4OAc	**4a**	80

[a] Isolated yields. [b] Starting material used was **3a**. [c] The reaction was performed with 5 g of **1a**.

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addition of *p*TSA (5 mol%) and after propargylation (60 min), NH_4OAc was added. We were pleased to see that the reaction proceeded efficiently to afford **4a** in 85% yield (Table 1, entry 11). Notably, this one-pot annulation was demonstrated by the synthesis of β-carboline **4a** on a gram scale (8.7 g, 80% yield) from 5 g of **1a** (Table 1, entry 12).

Having the optimized conditions in hand, diverse propargylic alcohols were first tested by reacting them with 2-formyl indole **1a** for one-pot sequential propargylation/aza-annulation reactions (Table 2). Propargylic alcohols bearing substituted phenyl at the C1-position **2b–2d** reacted efficiently with 1-methyl-1*H*-indole-2-carbaldehyde (**1a**) to afford the corresponding β-carbolines **4b–4d** in 89–91% yields. Next, heteroaryl (1-tosyl-1*H*-indol-3-yl) and alkenyl prop-2-yn-1-ols **2e** and **2f** were perfectly compatible in reacting with **1a** to give β-carbolines **4e** (93%) and **4f** (90%), respectively. Furthermore, propargyl alcohols bearing alkyl (**2g**) and cyclopropyl (**2h**) groups on the alkyne were used as the reaction partners with **1a** to afford the desired β-carbolines **4g** and **4h** in good yields. Interestingly, the propargyl alcohol bearing a silyl group on the alkyne, 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-ol (**2i**), was also compatible for the one-pot sequential propargylation/aza-annulation with **1a** to deliver the desilylated 3-methyl-β-carboline **4i** in 85% yield. Similarly, propargyl alcohol **2j** bearing *tert*-butyldimethylsilyl ether underwent the cyclization and desilylation to give the corresponding β-carboline **4j** in 92% yield.

Next, the feasibility of the use of 2,4-diyn-1-ols in this present protocol was also evaluated. Interestingly, the one-pot propargylation/annulation of 1,5-diphenylpenta-2,4-diyn-1-ol (**2k**) with **1a** in the presence of *p*TSA in acetonitrile followed by the addition of NH_4OAc delivered 3-allenyl-β-carboline **4k** in 70% yield (entry 1, Table 3) *via* the isomerization of the corresponding propargylated derivative to an allene towards the conjugation (may be due to the phenyl substitution on the alkyne). However, 1-phenylundeca-2,4-diyn-1-ol (**2l**) provided 3-propargyl-β-carboline **4l** in 76% yield (entry 2, Table 3) without isomerization to an allene due to the presence of the *n*-hexyl group on the alkyne. Encouraged by these results, we extended the scope of this one-pot reaction to indol-2-yl ketones **1b**, **1c** and we found that they were amenable to the reaction conditions, giving 1,3,5-trisubstituted β-carbolines **4m** (78%) and **4n** (81%), respectively (entries 3 and 4, Table 3). We were also glad to find that the *N*-unsubstituted indole-2-carbaldehyde (**1d**) underwent the propargylation with **2a** followed by aza-annulation under the optimized reaction conditions to afford 3-benzyl-4-phenyl β-carboline **4o** in 83% yield (entry 5, Table 3).

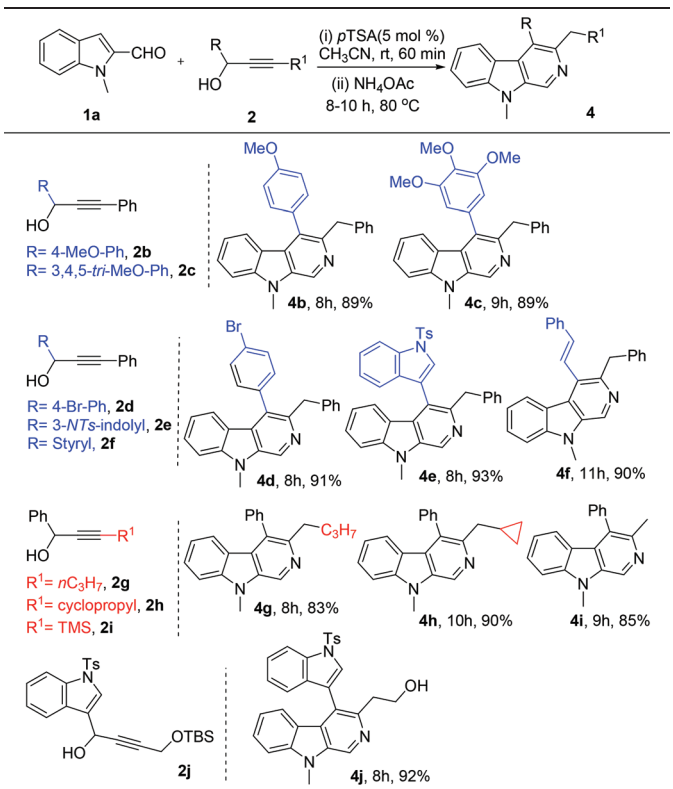
The versatility of this one-pot reaction was effectively explored with the substrate having two propargylic alcohol frameworks tethered to a phenyl ring **2m** with **1a** to furnish 1,4-bis(β-carbolinyl)-benzene **4p** in 87% yield (Scheme 2).

These results certainly greatly demonstrate the structural diversity of the resulting β-carboline compounds and show further synthetic manipulation sites as well. This was demonstrated by the bromination of **4a** to give 6-bromo-9-methyl-4-phenyl-9*H*-pyrido[3,4-*b*]indole (**5**) in 85% yield (Scheme 3), which can be further diversified using Pd-catalyzed cross-couplings. Compound **4a** was also converted to its *N*-oxide **6** in 90% yield (Scheme 3).

The aforementioned fruitful results encouraged us to extend the present metal-free one-pot approach for the synthesis of 5-azaindoles and 5-azabenzothiazoles, which are common structural motifs in a number of bioactive molecules.[19,20] Pyrrole 3-carboxaldehyde **7** was treated with propargylic alcohols **2a** and **2d** under the optimized conditions to obtain the corresponding 5-azaindoles **9a** (80%) and **9b** (86%), respectively (Table 4). Similarly, 5-azabenzothiazoles **10a** and **10b** were accessed from thiophene 3-carboxaldehyde **8** in good yields (Table 4).

On the basis of the above results and literature reports,[16c,21] a tentative mechanism for the described one-pot [4 + 2] annulation is proposed (Scheme 4). At the beginning, generation of carbocation **A** takes place from **2a** in the presence of *p*TSA and the addition of **1a** to **A** leads to propargylated indole **3a** *via* intermediate **B** involving C–C bond formation, and the condensation of protonated aldehyde **3a** with NH_4OAc as a nitrogen source results in the formation of imine **C**. The aza-cycloisomerisation of **C** to **4a** is possible *via* two ways: (a) through isomerization of the propargyl compound (**C**) to allene-intermediate **D** followed by C–N bond formation to **E** and aromati-

Table 2 Scope of propargylic alcohols[a]



[a] Reaction conditions: **1a** (1 mmol), **2** (1.2 mmol), *p*TSA (5 mol%), CH_3CN, rt, 60 min, then addition of NH_4OAc, 80 °C, 8–10 h.

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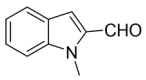
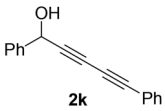
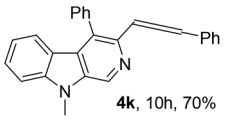
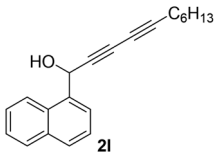
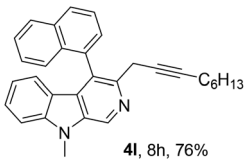
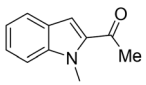
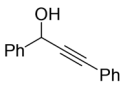
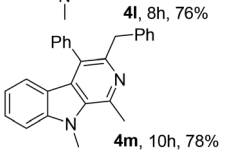
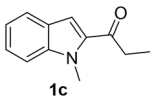
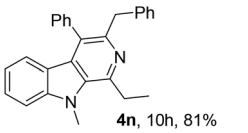
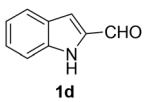
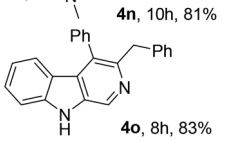
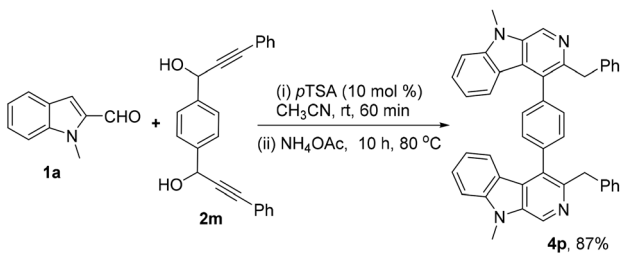
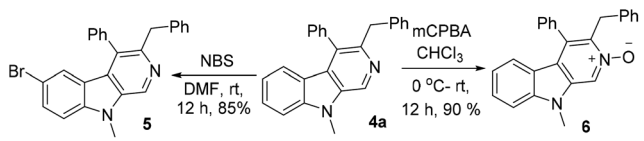
Table 3 Scope of indole-2-carbonyls[a]

Entry	Indole-2-carbonyl (1)	Propargyl alcohol (2)	β-Carboline[a] (4) Reaction time, yield[b]
1	 1a	 2k	 4k, 10h, 70%
2	1a	 2l	 4l, 8h, 76%
3	 1b	 2a	 4m, 10h, 78%
4	 1c	2a	 4n, 10h, 81%
5	 1d	2a	 4o, 8h, 83%

[a] Reaction conditions: **1** (1 mmol), **2** (1.2 mmol), pTSA (5 mol%), CH_3CN, rt, 60 min, and then addition of NH_4OAc, 80 °C, 8–10 h. [b] Isolated yields.

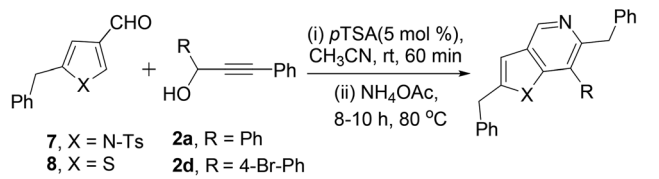


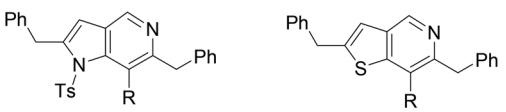
Scheme 2 Synthesis of 1,4-bis(β-carbolinyl)-benzene **4p**.



Scheme 3 Diversification of β-carboline **4a**.

Table 4 Synthesis of 5-azaindoles and 5-azabenzothiazoles





9a, R = Ph, 80%
9b, R = 4-Br-Ph, 86%

10a, R = Ph, 96%
10b, R = 4-Br-Ph, 90%

zation to **4a** and (b) direct intramolecular 6-*exo-dig*-cyclization of alkyne (**C**) with imine to **F** followed by isomerization to β-carboline **4a.**

After the development of the new synthetic methodology to access diversely substituted β-carbolines having either electron-releasing or withdrawing groups, we have carried out computational and photophysical studies.

Computational studies

Density functional theory (DFT) and time-dependent density functional theory (TDDFT) calculations were performed using the Gaussian 09 package with a functional basis set of the B3LYP/6-31G (d, p) to determine the orbital energy levels and oscillator strength values of β-carbolines (**4a-6**) in a vacuum (see the ESI, Tables S1, S2 and Fig. S1‡). Energy level diagrams show electron density on highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO) lying on the carboline moiety due to variations in the electronegativity of donor and acceptor moieties. The resultant

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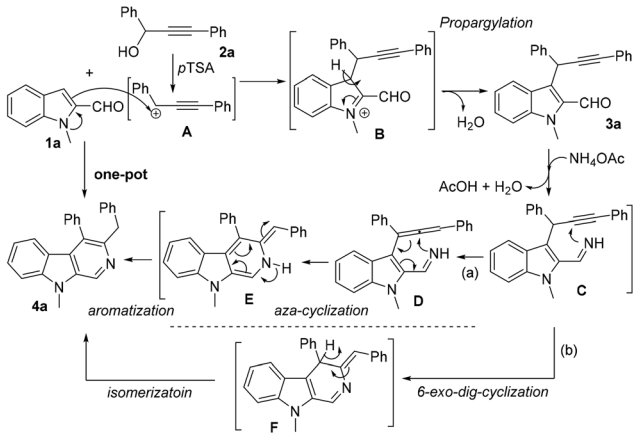

Scheme 4 Tentative reaction mechanism.

HOMO and LUMO values are in the range of −5.30 to −5.60 eV and −1.0 to −1.4 eV. The minimum band gap of each β-carboline observed in the range of 4.0–4.4 eV indicates that electron donors, acceptors and extension of π-conjugation influence the band gap of β-carboline systems, and thereby should allow possible fine-tuning of their opto-electronic properties for application in organic electronics (Fig. 2). In addition, DFT calculations clearly differentiate the electron density distribution in **4c** and **4j** leading to the possibilities of charge/energy or electron transfer.

However, β-carbolines consisting of *N*-oxide (**6**) exhibit a lower band gap compared to the –OH and –Br substituted derivatives.

Photophysical properties

UV-visible optical absorption studies of β-carboline derivatives were performed in chloroform at a concentration of 5×10^{-5} M. Absorption spectra of **4a**, **4c**, **4i**, **4e**, **4f**, and **4p** displayed the absorption maxima at 290 nm and 350 nm due to the phenyl groups at the 3-position of β-carbolines. However, **4d**, **4j**, and **6** possess strong electron withdrawing groups, bromides, alcohols and *N*-oxides, which affect the electrophilicity of the π-conjugated system thus resulting in a shift in absorption maxima towards the longer wavelength. Interestingly, the presence of a tosyl group in **4e** and **4j** extends the conjugation length of the molecule and the extent of absorption by approx. 50 nm, respectively. Thus, the excess/deficit of electron density plays a vital role in tuning the ground state electronic properties of the compounds (Fig. 3a).

Subsequently, emission studies were recorded at different excitation wavelengths of 290 and 365 nm.[22] The emission maxima of **4p**, **4c**, **4e**, and **4a** were recorded at 377, 380, 427 and 487 nm. However, electron withdrawing groups such as NO and –OH linked β-carboline derivatives showed an enhancement in the fluorescence intensity with the emission maxima being recorded at 402 and 435 nm, respectively (Fig. 3b and Fig. S2‡). Subsequently, quantum yields of these derivatives were observed in the range of 0.1–0.6 wherein

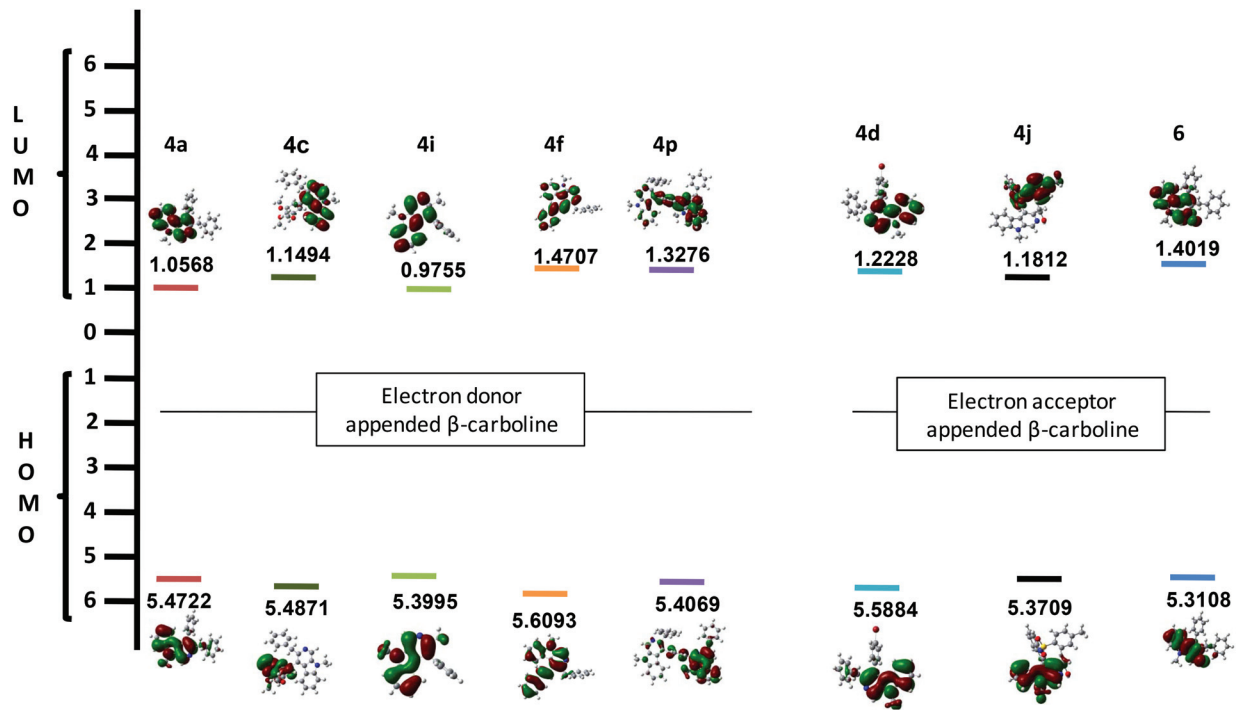

Fig. 2 HOMO–LUMO energy level diagram of β-carboline derivatives calculated by the B3LYP/6-31G (d, p) method. Note: Optimized structure and energy levels of **4e** not observed due to the steric hindrance of phenyl moieties.

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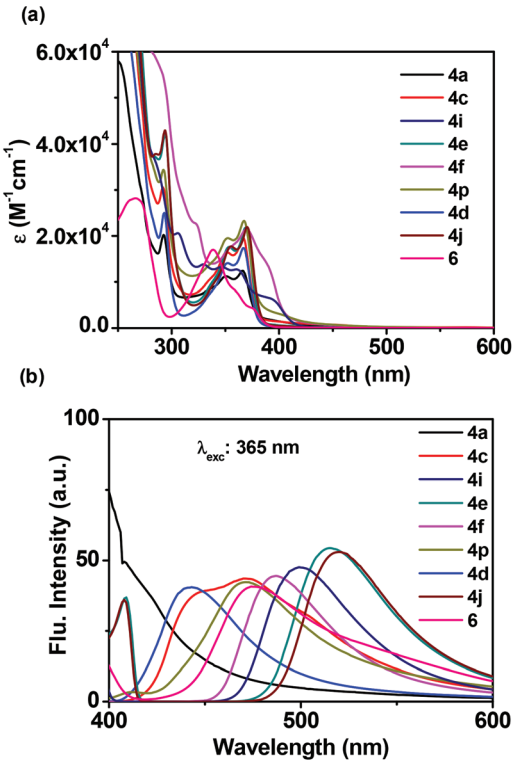

Fig. 3 (a) UV-Vis absorption spectra of β-carboline derivatives **4a-6** in $CHCl_3$ at a concentration of 5×10^{-5} M. (b) Emission studies of β-carboline derivatives in $CHCl_3$ at an excitation wavelength of 365 nm.

β-carbolines were used as a reference.[23] Thus, these results suggest that electron donating moieties constituting the β-carboline system exhibit blue emission, while similar molecules with electron withdrawing groups result in yellow and green emission. In addition, extension of conjugation plays a role in determining the electronic properties at the ground and excited state leading to long wavelength absorption and emission. UV-visible absorption and emission studies demonstrated the fine tuning of electronic properties by simple substitution of electron donors, acceptors and extension of π-conjugation.

Time correlated single photon counting (TCSPC) experiments were performed to evaluate the life time values of β-carboline systems upon substitution of various electron donors/acceptors in $CHCl_3$ using a 301 nm LED source. In the case of **4i** derivative, a monoexponential decay profile was observed with apparent values between 0.33 and 1.80 ns. Subsequently, addition of another methyl group and phenyl groups leads to an increase in lifetime values to 0.29, 2.20 ns and 4.18, 12.2 ns, respectively, due to an enhanced electron density in the π-conjugated system with a biexponential fit. However, molecules with electron acceptor moieties **6** and **4f** revealed the monoexponential profile with lifetime values of 3.58 ns. Thus, amongst the synthesized β-carbolines, **4f** and **6** exhibit a significant shift in absorption maxima and showed blue/green emission owing to the enhanced electron donating/withdrawing capabilities of Ph/–NO groups (Fig. 4). Nevertheless, the absorption spectra revealed no new band at a higher wavelength region, but the fluorescence spectra showed a considerable red shift compared to other derivatives and the lifetime data confirmed biexponential decay profile, suggesting that internal charge transfer is due to significant separation between donor and acceptor groups in **4c** and **4j**.

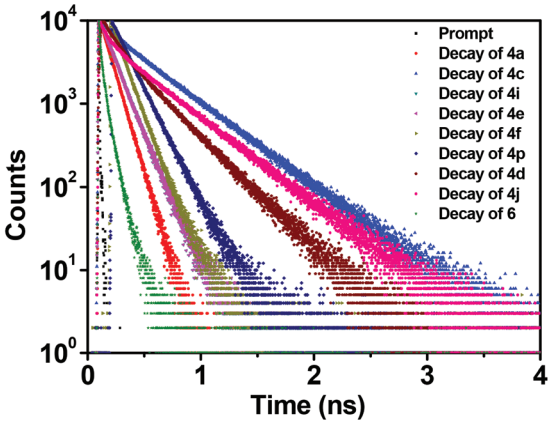

Fig. 4 Photoluminescence decay profile of β-carboline derivatives **4a-6** in $CHCl_3$ at an excitation wavelength of 301 nm LED source at 25 °C.

Electrochemical studies

The electrochemical properties of the β-carboline derivatives were determined in order to understand their redox behaviour by using supporting electrolyte (0.1 M NBu_4PF_6) with glassy carbon, calomel electrode, and platinum wire as the respective working, reference, and auxiliary electrodes at a scan rate of 200 mV s^{-1}. **4p** and **4c** show oxidation potentials at 1.10 V and 1.46 V and reduction potentials at −0.63 V and −0.78 V. **4i** shows oxidation potential at 0.69 V exclusively. **6**, **4d**, and **4f** exhibit oxidation potentials at around 1.48 V, 1.42 V and 0.66 V respectively. Tosyl group protected **6** and **4e** show intermediary reduction potentials at 1.29 V, −0.91, and −1.19 V respectively (Table 5, Fig. S2 and S3‡). Therefore, the electrochemical properties of β-carboline derivatives suggest the ease of oxidation for **4f** and **4i** exclusively due to presence of phenyl groups in β-carboline based π-conjugated systems.

Photostability studies

In order to investigate the stability of β-carboline derivatives, we illuminated the samples with an excitation wavelength (λ_{exc}) of 350 nm. In this regard, the samples were prepared in chloroform at a concentration of 5×10^{-5} M at 25 °C. UV-vis absorption spectra of β-carboline derivatives showed similar spectral characteristics prior to and after exposure to UV light for a time period of 1 h. The light exposed samples were recorded after 24 h and no significant changes in the absorption spectra were observed (Fig. 5). Thus, these studies confirmed that all the β-carboline derivatives with varying electron donating and withdrawing groups are photostable and their

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Table 5 Photophysical, electrochemical and band gap calculations of β-carboline derivatives

β-Carboline derivatives	λ_{abs} [a] (nm)	λ_{ems} [b] (nm)	τ [c] (ns)	Oxidation potential (V)	Reduction potential [d] (V)	Band gap [e] (eV)	ε [f] (M^{-1} cm^{-1})	Quantum yield (φ)
4a	292, 345, 365	377	2.64	1.30	−1.03	4.4154	2.0×10^4 (292 nm)	0.60
4c	292, 351, 366	377	0.29 2.20	1.465	−0.78	4.3377	3.0×10^4 (292 nm)	0.344
4i	305, 345, 361	427	1.80	0.69	−0.91	4.424	2.0×10^4 (305nm)	0.301
4e	292, 350, 367	514	4.18 12.2	1.26	−1.45	—	2.1×10^4 (367 nm)	0.302
4f	322, 369	436	3.58	0.66	−0.76	4.1386	2.1×10^4 (369 nm)	0.108
4p	292, 350, 367	380	0.33	1.10	−0.63	4.0793	3.4×10^4 (292nm)	0.218
4d	292, 350, 366	380	0.34 1.36	1.42	−1.12	4.3656	2.4×10^4 (292 nm)	0.106
4j	292, 350, 370	495	2.07 11.6	1.29	−1.19	4.1897	4.2×10^4 (292 nm)	0.499
6	265, 338	402	3.58	1.48	−0.91	3.9089	2.6×10^4 (265 nm)	0.490

[a] Absorption maximum values obtained from the spectra recorded in $CHCl_3$. [b] Emission maximum values from the fluorescence spectra measured in $CHCl_3$ at 25 °C. [c] Photoluminescence decay profiles analysed in $CHCl_3$ at 25 °C using a 301 nm LED source. [d] The redox potentials of dyes performed in $CHCl_3$ with 0.1 M tetrabutylammonium hexafluorophosphate ($TBAPF_6$) at a scan rate of 200 mV s^{-1} (*vs.* SCE). [e] Band gap obtained from the optimized structures using $E_{HOMO} - E_{LUMO}$. [f] Molar extinction co-efficient (ε) calculated by using concentration 5×10^{-5} M and path length: 1 cm.

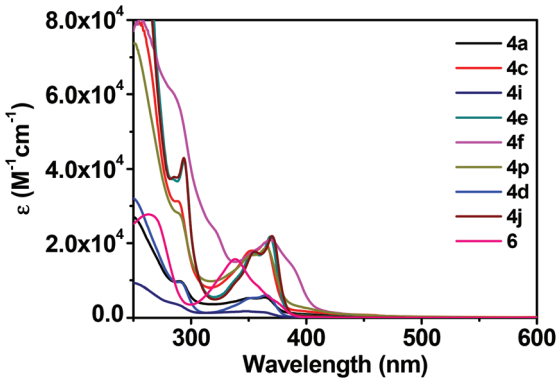

Fig. 5 UV-Vis absorption spectra of β-carboline derivatives in $CHCl_3$ upon exposure to UV light.

inherent electronic features remain unaffected during illumination.[24]

Conclusions

In summary, we have demonstrated a novel one-pot reaction to synthesize the diversely substituted β-carboline derivatives with electron-donor and acceptor moieties. This straightforward approach supplements the existing methods to access β-carbolines. Furthermore, the developed strategy was extended to the synthesis of 5-azaindoles and 5-azabenzothiazoles. Theoretical and photophysical properties suggested that compounds **4a-6** consisting of electron donor/acceptor moieties such as Ph and –NO on β-carboline systems strongly influenced their HOMO and LUMO energy levels which affects the ground and excited state electronic properties thereby leading to the extended absorption and blue or green emission observed. Cyclic voltammetric studies revealed that ease of redox behavior in **4f**, **4d** and **6** derivatives facilitates enhanced electron transport properties in these types of molecules. Therefore, optical and electrochemical properties of β-carboline systems could contribute to the design of novel carbolines for improving the performance of diverse LEDS and organic electronics.

Experimental

General methods

Oven-dried glass apparatus was used to perform all the reactions. The reactions were monitored by thin-layer chromatography carried out on silica plates using UV-light and anisaldehyde for visualization. Column chromatography was performed on silica gel (60–120 mesh) using *n*-hexane and ethyl acetate as eluents. Evaporation of solvents was done under reduced pressure at a temperature less than 45 °C. IR spectra were recorded using Perkin-Elmer 683 and Nicolet Nexus 670 spectrometers. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded in $CDCl_3$ solvent on a 300 MHz, 500 MHz and 400 MHz NMR spectrometer. Chemical shifts δ and coupling constants J are given in ppm (parts per million) and Hz (hertz) respectively. Chemical shifts are reported relative to residual solvent as an internal standard for ^1H and ^{13}C ($CDCl_3$: δ 7.26 ppm for ^1H and 77.0 ppm for ^{13}C). High resolution mass spectra (HRMS) [ESI^+] were obtained using either a TOF or a double focusing spectrometer, micro mass VG 70-70H or LC/MSD trap SL spectrometer operating at 70 eV using a direct inlet system.

2-Acyl indoles **1a**,[25] **1b**,[26] **1c**,[27] **1d**;[28] 3-formyl pyrrole **7**[16b] and 3-formyl thiophene **8**;[16b] and propargylic alcohols (**2a–2k**)[16a] and **2m**[29] were prepared using the literature procedures. Analytical data of all these compounds were correlated with the corresponding reported data.

1-(Naphthalen-1-yl)undeca-2,4-diyn-1-ol (2l)

To a stirred solution of 1-(naphthalen-1-yl)prop-2-yn-1-ol **Int-a**[30] (500 mg, 2.74 mmol) in dry toluene (10 mL) were added

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CuCl (15 mol%, 40 mg), $NH_2OH{\cdot}HCl$ (30 mol%, 56 mg), *n*-$BuNH_2$ (4.12 mmol, 0.4 mL), and 1-bromooct-1-yne[31] (4.12 mmol, 774 mg) (prepared using the known procedure given in ref. 8) at 0 °C, and the solution was warmed to room temperature and stirred for 2 h. The reaction mixture was quenched with 3N HCl and extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine (15 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography on silica gel (5% EtOAc in petroleum ether) to afford propargylic alcohol **2l** in 82% yield (652 mg). Pale brown viscous liquid, R_f = 0.5 (petroleum ether : EtOAc = 9 : 1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 8.5 Hz, 1H), 7.84 (dd, J = 8.4, 0.9 Hz, 1H), 7.78 (dd, J = 17.0, 7.6 Hz, 2H), 7.52 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.47 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H), 7.41 (dd, J = 8.2, 7.2 Hz, 1H), 6.08 (d, J = 5.9 Hz, 1H), 2.63 (dd, J = 6.0, 3.4 Hz, 1H), 2.25 (td, J = 7.0, 0.7 Hz, 2H), 1.54–1.46 (m, 2H), 1.39–1.32 (m, 2H), 1.30–1.21 (m, 4H), 0.87 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 134.9, 133.9, 130.3, 129.4, 128.7, 126.5, 125.9, 125.2, 124.7, 123.7, 82.8, 74.4, 72.4, 64.4, 63.3, 31.2, 28.4, 28.0, 22.4, 19.3, 14.0; IR (KBr): ν_{max} = 3361, 2929, 2252, 1457, 1223, 1003, 786 cm^{-1}; MS (ESI): m/z 313 $(M + Na)^+$; HRMS (EI): m/z calcd for $C_{21}H_{22}O$ $(M)^+$: 290.1670, found: 290.1663.

3-(1,3-Diphenylprop-2-yn-1-yl)-1-methyl-1*H*-indole-2-carbaldehyde (3a)

A solution of **1a** (100 mg, 0.62 mmol) in acetonitrile at room temperature was allowed to react with 1,3-diphenylprop-2-yn-1-ol (**2a**, 156 mg, 0.75 mmol) and *p*TSA (5 mg, 0.03 mmol). After 30 min, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (5% EtOAc in petroleum ether) to afford propargylated indole **3a** in 95% yield (207 mg). Pale yellow solid, mp 118–120 °C, R_f = 0.5 (petroleum ether : EtOAc = 1 : 9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (s, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.56 (d, J = 7.9 Hz, 2H), 7.49–7.43 (m, 2H), 7.42–7.35 (m, 2H), 7.35–7.28 (m, 5H), 7.23 (t, J = 7.3 Hz, 1H), 7.14 (ddd, J = 8.0, 6.5, 1.3 Hz, 1H), 6.07 (s, 1H), 4.09 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.3, 140.4, 139.7, 131.7, 130.5, 128.6, 128.3, 128.2, 127.3, 127.2, 127.0, 125.1, 123.1, 122.3, 120.8, 110.4, 89.2, 85.0, 33.2, 31.8; IR (KBr) ν_{max} = 3060, 1659, 1479, 1203, 889, 747, 699 cm^{-1}; MS (ESI): m/z 372 $(M + Na)^+$; HRMS (ESI): m/z calcd for $C_{25}H_{19}NONa$ $(M + Na)^+$: 372.1364, found: 372.1364.

General procedure for the one-pot synthesis of β-carbolines (4a–4o)

To a stirred solution of 2-acyl indole **1** (1.0 mmol) and propargylic alcohol **2** (1.2 mmol) in 10 mL of acetonitrile was added *p*TSA (5 mol%) at room temperature and stirred for 60 min. Then, NH_4OAc (1.2 mmol) was added to the reaction mixture and stirred at 80 °C in a silicone oil bath for 8–11 h. After the completion of the reaction (monitored by TLC) the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (EtOAc–hexanes) to afford the corresponding β-carboline products (for reaction times and yields of products, see Schemes 2–3 and Tables 2–4).

3-Benzyl-9-methyl-4-phenyl-9*H*-pyrido[3,4-*b*] indole (4a)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2a** (156 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4a** in 85% yield (183 mg). Yellow solid, mp 126–128 °C, R_f = 0.5 (petroleum ether : EtOAc = 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.53–7.45 (m, 4H), 7.40 (d, J = 8.3 Hz, 1H), 7.33–7.29 (m, 2H), 7.16 (t, J = 7.3 Hz, 2H), 7.10 (t, J = 7.2 Hz, 1H), 7.03 (d, J = 7.1 Hz, 2H), 6.93 (t, J = 7.2 Hz, 1H), 6.87 (d, J = 7.9 Hz, 1H), 4.18 (s, 2H), 3.95 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 145.2, 143.1, 139.7, 136.4, 135.4, 131.3, 129.4, 129.2, 129.0, 128.9, 128.5, 128.2, 127.5, 126.0, 123.8, 120.8, 120.1, 109.2, 39.2, 29.7; IR (KBr): ν_{max} = 3058, 2925, 2360, 1451, 752, 702 cm^{-1}; MS (ESI): m/z 349 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{25}H_{21}N_2$ $(M + H)^+$: 349.1699, found: 349.1714.

3-Benzyl-4-(4-methoxyphenyl)-9-methyl-9*H*-pyrido[3,4-*b*]indole (4b)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2b** (175 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4b** in 89% yield (208 mg). Pale yellow liquid, R_f = 0.5 (petroleum ether : EtOAc = 1 : 1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.49 (ddd, J = 8.2, 5.1, 3.1 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.24–7.09 (m, 5H), 7.04 (d, J = 8.4 Hz, 4H), 6.97 (d, J = 2.8 Hz, 2H), 4.19 (s, 2H), 3.94 (s, 3H), 3.94 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.2, 147.7, 142.1, 141.5, 135.7, 130.6, 130.2, 130.1, 128.8, 128.2, 128.0, 127.8, 125.6, 123.5, 121.3, 119.2, 114.2, 108.8, 55.3, 40.7, 29.3; IR (KBr): ν_{max} = 2928, 2360, 1612, 1507, 1246, 1033, 749 cm^{-1}; MS (ESI): m/z 379 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{26}H_{23}N_2O$ $(M + H)^+$: 379.1791, found: 379.1789.

3-Benzyl-9-methyl-4-(3,4,5-trimethoxyphenyl)-9*H*-pyrido-[3,4-*b*] indole (4c)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2c** (224 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4c** in 89% yield (241 mg). Pale brown liquid, R_f = 0.5 (petroleum ether : EtOAc = 7 : 3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.56–7.48 (m, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.20–7.13 (m, 2H), 7.10 (d, J = 7.0 Hz, 1H), 7.07–6.97 (m, 4H), 6.43 (s, 2H), 4.23 (s, 2H), 3.99 (s, 3H), 3.96 (s, 3H), 3.67 (s, 6H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 153.4, 147.1, 142.2, 141.6, 137.5, 135.7, 133.1, 130.4, 130.0, 128.7, 128.1, 128.0, 125.6, 123.6, 121.0, 119.5, 108.9, 106.3, 61.1, 56.0, 41.1, 29.4; IR (KBr): ν_{max} = 2926, 1447, 1369, 1174, 1369, 751, 665 cm^{-1}; MS (ESI): m/z 439 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{28}H_{27}N_2O_3$ $(M + H)^+$: 439.2016, found: 439.2014.

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3-Benzyl-4-(4-bromophenyl)-9-methyl-9*H*-pyrido[3,4-*b*]-indole (4d)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2d** (214 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4d** in 91% yield (240 mg). Light green solid, mp 150–152 °C, R_f = 0.5 (petroleum ether : EtOAc = 1 : 1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 7.66–7.61 (m, 2H), 7.50 (ddd, J = 8.3, 5.6, 1.3 Hz, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.17 (ddd, J = 7.7, 4.1, 1.9 Hz, 4H), 7.13–7.08 (m, 1H), 7.04–6.97 (m, 3H), 6.93 (d, J = 7.9 Hz, 1H), 4.16 (s, 2H), 3.95 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 146.6, 142.4, 140.7, 136.6, 135.6, 132.0, 131.8, 131.2, 130.5, 129.9, 129.2, 128.7, 128.4, 128.2, 125.8, 123.3, 122.2, 120.8, 120.3, 119.6, 109.1, 40.4, 29.5; IR (KBr): ν_{max} = 2359, 1489, 1447, 1072, 826, 752, 705 cm^{-1}; MS (ESI): m/z 427 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{25}H_{20}BrN_2$ $(M + H)^+$: 427.0804, found: 427.0823.

3-Benzyl-9-methyl-4-(1-tosyl-1*H*-indol-2-yl)-9*H*-pyrido[3,4-*b*]-indole (4e)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2e** (302 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4e** in 93% yield (311 mg). Light brown solid, mp 228–230 °C, R_f = 0.5 (petroleum ether : EtOAc = 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 8.4 Hz, 2H), 7.52 (s, 1H), 7.46–7.35 (m, 3H), 7.20 (d, J = 8.1 Hz, 2H), 7.12–7.03 (m, 4H), 6.87 (t, J = 7.3 Hz, 3H), 6.65 (ddd, J = 19.2, 13.0, 4.4 Hz, 2H), 4.18 (d, J = 14.7 Hz, 1H), 4.01 (d, J = 14.7 Hz, 1H), 3.96 (s, 3H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.0, 145.0, 142.1, 141.1, 135.6, 135.2, 135.1, 131.1, 130.6, 129.9, 128.8, 128.5, 128.1, 128.0, 126.9, 125.7, 125.2, 124.7, 123.7, 123.2, 120.7, 120.5, 120.1, 120.0, 119.3, 114.0, 108.9, 41.1, 29.4, 21.6; IR (KBr): ν_{max} = 2360, 1446, 1370, 1174, 1123, 750 cm^{-1}; MS (ESI): m/z 542 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{34}H_{28}N_3O_2S$ $(M + H)^+$: 542.1897, found: 542.1923.

(*E*)-3-Benzyl-9-methyl-4-styryl-9*H*-pyrido[3,4-*b*]indole (4f)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2f** (176 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4f** in 90% yield (208 mg). Pale yellow liquid, R_f = 0.3 (petroleum ether : EtOAc = 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.59–7.51 (m, 4H), 7.44 (dd, J = 13.0, 5.8 Hz, 3H), 7.38–7.31 (m, 2H), 7.25–7.21 (m, 3H), 7.16 (dt, J = 7.2, 5.2 Hz, 2H), 6.92 (d, J = 16.6 Hz, 1H), 4.46 (s, 2H), 3.94 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 147.5, 142.2, 141.1, 136.9, 136.0, 135.9, 129.7, 128.9, 128.8, 128.3, 128.1, 127.9, 127.3, 127.0, 126.6, 125.8, 124.2, 124.0, 121.4, 119.4, 109.0, 41.4, 29.4; IR (KBr): ν_{max} = 3027, 2359, 1612, 1485, 1447, 748, 700 cm^{-1}; MS (ESI): m/z 375 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{27}H_{23}N_2$ $(M + H)^+$: 375.1856, found: 375.1859.

3-Butyl-9-methyl-4-phenyl-9*H*-pyrido[3,4-*b*] indole (4g)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2g** (131 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4g** in 83% yield (161 mg). Light yellow liquid, R_f = 0.5 (petroleum ether : EtOAc = 7 : 3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.84 (s, 1H), 7.62–7.41 (m, 5H), 7.40–7.34 (m, 2H), 6.93 (t, J = 7.4 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 3.92 (s, 3H), 2.80–2.72 (t, 2H), 1.73–1.59 (m, 2H), 1.33–1.25 (m, 2H), 0.81 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 149.1, 142.1, 138.4, 135.4, 130.1, 129.6, 129.3, 128.8, 127.7, 123.4, 121.2, 119.1, 108.7, 34.4, 33.1, 29.3, 22.7, 13.9; IR (KBr): ν_{max}: 2925, 2861, 1447, 1295, 1031, 747, 702 cm^{-1}; MS (ESI): m/z 315 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{22}H_{22}N_2Na$ $(M + Na)^+$: 337.1675, found: 337.1686.

3-(Cyclopropylmethyl)-9-methyl-4-phenyl-9*H*-pyrido[3,4-*b*] indole (4h)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2h** (129 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4h** in 90% yield (174 mg). Pale yellow liquid; R_f = 0.5 (petroleum ether : EtOAc = 7 : 3); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.88 (s, 1H), 7.58–7.51 (m, 3H), 7.49 (ddd, J = 8.2, 6.4, 2.9 Hz, 1H), 7.43–7.39 (m, 3H), 6.95–6.91 (m, 1H), 6.83 (d, J = 7.9 Hz, 1H), 3.96 (s, 3H), 2.71 (d, J = 6.8 Hz, 2H), 1.13–1.06 (m, 1H), 0.42–0.35 (m, 2H), 0.11–0.07 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 148.4, 142.2, 138.3, 135.4, 129.9, 129.6, 129.5, 128.8, 127.9, 127.8, 123.4, 121.2, 119.2, 108.8, 38.9, 29.4, 11.7, 4.6; IR (KBr): ν_{max} = 2926, 1620, 1446, 1020, 749, 702 cm^{-1}; MS (ESI): m/z 313 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{22}H_{21}N_2$ $(M + H)^+$: 313.1699, found: 313.1712.

3,9-Dimethyl-4-phenyl-9*H*-pyrido[3,4-*b*] indole (4i)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2i** (153 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4i** in 85% yield (143 mg). Yellow solid, mp 88–90 °C, R_f = 0.5 (petroleum ether : EtOAc = 7 : 3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (s, 1H), 7.59–7.52 (m, 3H), 7.48 (dd, J = 8.3, 4.2 Hz, 1H), 7.42–7.38 (m, 3H), 6.97–6.92 (m, 2H), 3.94 (s, 3H), 2.50 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 144.9, 142.2, 138.6, 135.7, 129.8, 129.6, 129.1, 128.9, 127.8, 127.7, 123.4, 121.0, 119.1, 108.8, 29.3, 21.9; IR (KBr): ν_{max} = 3052, 2924, 1619, 1447, 1025, 748, 700 cm^{-1}; MS (ESI): m/z 272 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{19}H_{17}N_2$ $(M + H)^+$: 273.1386, found: 273.1384.

2-(9-Methyl-4-(1-tosyl-1*H*-indol-2-yl)-9*H*-pyrido [3,4-*b*] indol-3-yl) ethan-1-ol (4j)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2j** (353 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the

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addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4j** in 92% (284 mg). Pale yellow solid, mp 130–132 °C, R_f = 0.5 (petroleum ether : EtOAc = 2 : 8); ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.21 (d, J = 8.4 Hz, 1H), 7.91–7.82 (m, 2H), 7.67 (s, 1H), 7.52–7.37 (m, 3H), 7.33–7.23 (m, 2H), 7.21–7.09 (m, 1H), 7.06–6.98 (m, 1H), 6.71–6.63 (m, 2H), 3.97 (s, 3H), 3.92–3.87 (m, 2H), 2.99–2.78 (m, 2H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.3, 145.2, 142.6, 135.5, 135.3, 130.2, 130.0, 129.3, 128.7, 126.9, 125.5, 124.9, 124.0, 123.3, 120.3, 119.6, 119.2, 114.2, 109.1, 62.2, 34.9, 29.5, 21.6; IR (KBr): ν_{max} = 2925, 2359, 1175, 759, 669 cm^{-1}; MS (ESI): m/z 496 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{29}H_{26}N_3O_3S$ $(M + H)^+$: 496.1687, found: 496.1695.

9-Methyl-4-phenyl-3-(3-phenylpropa-1,2-dien-1-yl)-9*H*-pyrido[3,4-*b*]indole (4k)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2k** (175 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4k** in 70% yield (162 mg). Brown viscous liquid, R_f = 0.6 (petroleum ether : EtOAc = 4 : 1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 7.59–7.55 (m, 1H), 7.51–7.47 (m, 4H), 7.45–7.43 (m, 1H), 7.39 (s, 1H), 7.32–7.27 (m, 3H), 7.25 (d, J = 1.5 Hz, 1H), 7.18–7.13 (m, 1H), 6.98–6.94 (m, 2H), 6.75 (d, J = 6.6 Hz, 1H), 6.49 (d, J = 6.6 Hz, 1H), 3.93 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 209.5, 142.0, 140.4, 137.6, 135.6, 134.1, 131.3, 129.7, 129.6, 129.5, 128.9, 128.8, 128.4, 128.0, 127.9, 127.5, 127.0, 126.8, 123.4, 121.1, 119.5, 109.0, 97.6, 97.5, 29.3; IR (KBr): ν_{max} = 3058, 1639, 1454, 1253, 958, 748 cm^{-1}; MS (ESI): m/z 373 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{27}H_{21}N_2$ $(M + H)^+$: 373.1705, found: 373.1703.

9-Methyl-4-(naphthalen-1-yl)-3-(non-2-yn-1-yl)-9*H*-pyrido- [3,4-*b*]indole (4l)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile at room temperature was allowed to react with **2l** (218 mg, 0.75 mmol) in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4l** in 76% yield (203 mg). Pale red viscous liquid, R_f = 0.3 (petroleum ether : EtOAc = 7 : 3); ^1H NMR (500 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.04 (d, J = 8.3 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.65 (dd, J = 8.2, 7.0 Hz, 1H), 7.56 (dd, J = 7.0, 1.1 Hz, 1H), 7.49–7.44 (m, 1H), 7.41–7.34 (m, 3H), 7.25–7.21 (m, 1H), 6.73 (ddd, J = 8.0, 6.7, 1.4 Hz, 1H), 6.40 (d, J = 8.0 Hz, 1H), 3.96 (s, 3H), 3.64 (dt, J = 17.2, 2.4 Hz, 1H), 3.55 (dt, J = 17.2, 2.4 Hz, 1H), 2.03 (tt, J = 7.2, 2.3 Hz, 2H), 1.38–1.31 (m, 2H), 1.28–1.17 (m, 6H), 0.84 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 145.0, 142.1, 135.9, 135.0, 133.7, 131.8, 130.8, 128.6, 128.5, 128.2, 127.8, 127.4, 127.2, 126.3, 126.1, 125.7, 125.6, 123.2, 120.9, 119.3, 108.8, 81.9, 77.8, 31.3, 29.4, 28.8, 28.5, 25.5, 22.5, 18.9, 14.0; IR (KBr): ν_{max} = 2926, 1618, 1449, 1335, 1251, 1011, 749 cm^{-1}; MS (ESI): m/z 431 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{31}H_{31}N_2$ $(M + H)^+$: 431.2487, found: 431.2484.

3-Benzyl-1,9-dimethyl-4-phenyl-9*H*-pyrido[3,4-*b*]indole (4m)

Following the general procedure, 1-(1-methyl-1*H*-indol-2-yl) ethanone **1b** (100 mg, 0.58 mmol) in acetonitrile at room temperature was allowed to react with **2a** (144 mg, 0.69 mmol) and *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (53 mg, 0.69 mmol) to afford compound **4m** in 78% yield (164 mg). Light brown solid, mp 110–112 °C, R_f = 0.5 (petroleum ether : EtOAc = 7 : 3); ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.43 (m, 4H), 7.38 (d, J = 8.2 Hz, 1H), 7.23 (d, J = 3.8 Hz, 2H), 7.19–7.07 (m, 3H), 7.05–6.99 (m, 2H), 6.93–6.85 (m, 1H), 6.74 (d, J = 8.0 Hz, 1H), 4.16 (s, 3H), 4.11 (s, 2H), 3.15 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 146.1, 142.5, 141.4, 140.1, 138.2, 134.5, 129.6, 128.8, 128.7, 128.6 (2C), 128.2, 127.8, 127.6, 127.4, 125.4, 123.2, 121.3, 119.1, 109.0, 40.6, 32.2, 23.8; IR (KBr): ν_{max} = 3026, 1610, 1439, 1300, 908, 734, 702 cm^{-1}; MS (ESI): m/z 363 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{26}H_{23}N_2$ $(M + H)^+$: 363.1861, found: 363.1863.

3-Benzyl-1-ethyl-9-methyl-4-phenyl-9*H*-pyrido[3,4-*b*]indole (4n)

Following the general procedure, **1c** (100 mg, 0.53 mmol) in acetonitrile was allowed to react with **2a** (133 mg, 0.64 mmol) in the presence of *p*TSA (4 mg, 0.03 mmol) followed by the addition of NH_4OAc (49 mg, 0.64 mmol) to afford β-carboline **4n** in 81% yield (161 mg). Pale yellow viscous liquid, R_f = 0.5 (petroleum ether : EtOAc = 4 : 1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.45 (m, 3H), 7.44–7.41 (m, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.25–7.22 (m, 2H), 7.14 (ddd, J = 7.4, 4.4, 1.4 Hz, 2H), 7.09 (dt, J = 5.2, 2.1 Hz, 1H), 7.05 (dd, J = 6.5, 5.0 Hz, 2H), 6.88 (ddd, J = 8.0, 6.9, 1.1 Hz, 1H), 6.75–6.72 (m, 1H), 4.13 (s, 3H), 4.11 (s, 2H), 3.45 (q, J = 7.5 Hz, 2H), 1.52 (t, J = 7.5 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 146.1, 145.3, 142.6, 141.4, 138.3, 133.6, 129.7, 128.8, 128.6 (2C), 128.3, 127.8, 127.6, 127.4, 125.4, 123.2, 121.4, 119.1, 109.0, 40.6, 32.2, 29.0, 14.8; IR (KBr): ν_{max} = 3061, 1659, 1448, 1257, 1030, 752, 702 cm^{-1}; MS (ESI): m/z 377 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{27}H_{25}N_2$ $(M + H)^+$: 377.2018, found: 377.2021.

3-Benzyl-4-phenyl-9*H*-pyrido[3,4-*b*]indole (4o)

Following the general procedure, **1d** (100 mg, 0.69 mmol) in acetonitrile was allowed to react with **2a** (171 mg, 0.82 mmol) in the presence of *p*TSA (5.9 mg, 0.03 mmol) followed by the addition of NH_4OAc (49 mg, 0.64 mmol) to afford β-carboline **4o** in 83% yield (191 mg). Yellow liquid, R_f = 0.5 (petroleum ether : EtOAc = 1 : 1); ^1H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.39 (s, 1H), 7.54–7.48 (m, 3H), 7.46–7.39 (m, 2H), 7.33 (ddd, J = 5.5, 4.9, 3.5 Hz, 2H), 7.17 (dd, J = 7.9, 6.5 Hz, 2H), 7.10 (dd, J = 8.6, 5.9 Hz, 1H), 7.06–7.01 (m, 2H), 6.94 (ddd, J = 8.1, 6.1, 2.0 Hz, 1H), 6.85 (d, J = 8.0 Hz, 1H), 4.17 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 147.5, 141.2, 140.8, 137.9, 134.4, 132.1, 130.5, 129.5, 128.8, 128.1, 128.03, 127.9, 125.6, 123.4, 121.7, 119.8, 111.2, 40.7; IR (KBr): ν_{max} = 3026, 1616.62, 1435, 1331, 750, 701 cm^{-1}; MS (ESI): m/z 335 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{24}H_{19}N_2$ $(M + H)^+$: 335.1551, found: 335.1548.

1,4-Bis(3-benzyl-5-methyl-5*H*-pyrido[4,3-*b*]indol-4-yl)-benzene (4p)

Following the general procedure, **1a** (100 mg, 0.62 mmol) in acetonitrile was allowed to react with **2m** (125 mg, 0.37 mmol)

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in the presence of *p*TSA (5 mg, 0.03 mmol) followed by the addition of NH_4OAc (58 mg, 0.75 mmol) to afford β-carboline **4p** in 60% yield (229 mg). Yellow solid, mp 130–132 °C, R_f = 0.5 (DCM : methanol = 9.5 : 0.5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.96 (s, 1H), 7.59–7.51 (m, 2H), 7.49 (s, 1H), 7.47 (s, 4H), 7.46 (s, 1H), 7.45 (d, J = 3.5 Hz, 1H), 7.42 (s, 1H), 7.21 (d, J = 7.0 Hz, 3H), 7.17–7.08 (m, 8H), 7.01–6.96 (m, 1H), 4.39 (s, 2H), 4.33 (s, 2H), 4.01 (s, 3H), 4.00 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 147.5, 146.9, 142.3, 141.2, 137.7, 135.8, 132.1, 130.4, 130.1, 128.8, 128.7, 128.3, 128.2, 125.8, 123.5, 123.3, 121.2, 119.3, 109.1, 41.0, 29.5; IR (KBr) ν_{max} = 1446, 1236, 987, 845, 751 cm^{-1}; MS (ESI): m/z 619 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{44}H_{35}N_4$ $(M + H)^+$: 619.2856, found: 619.2850.

3-Benzyl-6-bromo-9-methyl-4-phenyl-9*H*-pyrido[3,4-*b*]-indole (5)

To a stirred solution of 3-benzyl-9-methyl-4-phenyl-9*H*-pyrido [3,4-*b*]indole (**4a**, 50 mg 0.14 mmol), *N*,*N*-dimethylformamide (10 mL) was added to a round bottomed flask followed by slow addition of *N*-bromosuccinamide (30 mg, 0.17 mmol). The reaction was carried out at room temperature for 12 hours, and then water was added, followed by extraction with ethyl acetate (2 times). The crude product was purified by column chromatography on silica gel (EtOAc–hexane) to afford the corresponding compound **5** in 85% yield (50 mg). Pale yellow liquid, R_f = 0.5 (petroleum ether : EtOAc = 1 : 1); ^{1}H NMR (400 MHz) δ 8.89 (s, 1H), 7.57–7.51 (m, 4H), 7.30–7.26 (m, 3H), 7.20–7.14 (m, 2H), 7.10 (ddd, J = 7.3, 3.7, 1.4 Hz, 1H), 7.05–7.01 (m, 2H), 6.93 (t, J = 1.9 Hz, 1H), 4.18 (s, 2H), 3.93 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 147.6, 141.0, 140.7, 137.3, 135.8, 130.7, 130.6, 129.2, 128.9, 128.8, 128.2, 128.1, 127.0, 126.0, 125.7, 122.8, 112.0, 110.3, 40.6, 29.5; IR (KBr): ν_{max} = 1709, 1460, 1289, 1065, 753, 704 cm^{-1}; MS (ESI): m/z 427 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{25}H_{19}BrN_2$ $(M + H)^+$: 427.0810, found: 427.0847.

3-Benzyl-9-methyl-4-phenyl-9*H*-pyrido[3,4-*b*] indole 2-oxide (6)

To a stirred solution of 3-benzyl-9-methyl-4-phenyl-9*H*-pyrido [3,4-*b*] indole (**4a**, 50 mg, 0.143 mmol) in $CHCl_3$ (10 mL) was added 70% *m*-CPBA (31 mg, 0.14 mmol), portion wise at 0 °C. The mixture was stirred at room temperature for 12 h after the completion of the reaction (monitored by TLC). The reaction mixture was diluted with $CHCl_3$, and solid K_2CO_3 (4.0 equiv.) was added. The resulting mixture was stirred for an additional 10 min. The crude product was purified by column chromatography on silica gel (DCM : methanol) to afford the corresponding compound **6** in 90% (46 mg). Pale yellow solid, mp 108–110 °C, R_f = 0.5 (DCM : methanol = 9.5 : 0.5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.56–7.49 (m, 3H), 7.48–7.42 (m, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.32–7.28 (m, 2H), 7.20–7.12 (m, 3H), 7.12–7.04 (m, 3H), 6.95 (t, 1H), 6.72 (d, J = 8.0 Hz, 1H), 4.32 (s, 2H), 3.84 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 142.9, 141.0, 138.8, 136.5, 135.9, 133.2, 129.1, 129.0, 128.7, 128.3, 128.1, 127.6, 125.9, 122.4, 121.6, 121.3, 120.3, 108.8, 33.3, 29.6; IR (KBr): ν_{max} = 1225, 1162, 1003, 748, 701 cm^{-1}; MS (ESI): m/z 365 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{25}H_{21}N_2O$ $(M + H)^+$: 365.1661, found: 365.1656.

General procedure for 5-azaindoles and 5-azabenzothiazoles (9a, 9b and 10a, 10b)

To a stirred solution of 3-formyl pyrrole or 3-formyl thiophene (1.0 mmol) and propargylic alcohol (1.2 mmol) in 10 mL of acetonitrile was added *p*TSA (5 mol%) at room temperature and stirred for 30–60 min. Then, NH_4OAc (1.2 mmol) was added to the reaction mixture at rt and continuously stirred at 80 °C for 8–10 h. After the completion of the reaction (monitored by TLC) the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (EtOAc–hexanes) to afford the corresponding 5-azaindoles and 5-azabenzothiazoles respectively (Table 4).

2,6-Dibenzyl-7-phenyl-1-tosyl-1*H*-pyrrolo[3,2-*c*] pyridine (9a)

Following the general procedure, **7** (100 mg, 0.25 mmol) in acetonitrile was allowed to react with **2a** (64 mg, 0.30 mmol) in the presence of *p*TSA (2.2 mg, 0.01 mmol) followed by the addition of NH_4OAc (23 mg, 0.30 mmol) to afford 5-azaindole **9a** in 80% yield (105 mg). Yellow solid, mp 180–182 °C, R_f = 0.5 (petroleum ether : EtOAc = 8 : 2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.34–7.27 (m, 3H), 7.20 (dd, J = 10.0, 4.3 Hz, 3H), 7.13–7.03 (m, 5H), 7.00–6.92 (m, 6H), 6.81 (d, J = 6.8 Hz, 2H), 6.27 (s, 1H), 4.32 (s, 2H), 3.96 (s, 2H), 2.34 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 154.8, 145.8, 143.9, 143.6, 141.6, 140.4, 137.9, 136.9, 136.4, 130.8, 129.5, 129.4, 128.7, 128.6, 127.9, 127.3, 126.9, 126.4, 125.7, 125.6, 110.7, 41.9, 36.6, 21.5; IR (KBr): ν_{max} = 3030, 1412, 1362, 1176, 1010, 749, 666 cm^{-1}; MS (ESI): m/z 529 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{34}H_{29}N_2O_2S$ $(M + H)^+$: 529.1944, found: 529.1931.

2,6-Dibenzyl-7-(4-bromophenyl)-1-tosyl-1*H*-pyrrolo[3,2-*c*] pyridine (9b)

Following the general procedure, **7** (100 mg, 0.25 mmol) in acetonitrile was allowed to react with **2d** (88 mg, 0.31 mmol) in the presence of *p*TSA (2.2 mg, 0.01 mmol) followed by the addition of NH_4OAc (23 mg, 0.30 mmol) to afford 5-azaindole **9b** in 86% yield (130 mg). Pale yellow solid, mp 180–182 °C, R_f = 0.5 (petroleum ether : EtOAc = 8 : 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.36–7.28 (m, 3H), 7.23 (dd, J = 7.6, 1.7 Hz, 2H), 7.12–7.04 (m, 3H), 7.00 (dd, J = 8.1, 5.9 Hz, 4H), 6.82–6.76 (m, 4H), 6.68 (d, J = 8.4 Hz, 2H), 6.40 (s, 1H), 4.38 (s, 2H), 3.91 (s, 2H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.4, 145.9, 143.9, 143.5, 141.9, 140.1, 137.9, 136.8, 135.1, 132.6, 130.0, 129.6, 129.3, 128.7, 128.5, 128.0, 126.9, 126.3, 125.7, 125.0, 121.9, 110.4, 41.9, 36.6, 21.5; IR (KBr): ν_{max} = 1592, 1411, 1368, 1182, 997, 765, 702 cm^{-1}; MS (ESI): m/z 607 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{34}H_{28}BrN_2O_2S$ $(M + H)^+$: 607.1055, found: 607.1049.

2,6-Dibenzyl-7-phenylthieno[3,2-*c*] pyridine (10a)

Following the general procedure, **8** (100 mg, 0.39 mmol) in acetonitrile was allowed to react with **2a** (99 mg, 0.47 mmol) in the presence of *p*TSA (3.4 mg, 0.02 mmol) followed by the addition of NH_4OAc (36.6 mg, 0.47 mmol) to afford 5-azabenzo-

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thiazole **10a** in 96% yield (146 mg). Brown liquid, R_f = 0.5 (petroleum ether : EtOAc = 7 : 3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.43 (dd, J = 5.1, 1.8 Hz, 3H), 7.29 (dd, J = 6.8, 2.6 Hz, 4H), 7.23 (d, J = 4.3 Hz, 2H), 7.14 (dd, J = 11.4, 6.3 Hz, 4H), 7.00 (d, J = 6.7 Hz, 2H), 4.16 (s, 2H), 4.13 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.2, 149.9, 147.1, 143.3, 140.5, 138.9, 137.7, 134.9, 130.6, 129.1, 128.7, 128.2, 128.1, 126.9, 125.8, 120.0, 41.0, 37.0; IR (KBr): ν_{max} = 3028, 1493, 1362, 1178, 761, 699, 671 cm^{-1}; MS (ESI): m/z 392 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{27}H_{22}NS$ $(M + H)^+$: 392.1467, found: 392.1488.

2,6-Dibenzyl-7-(4-bromophenyl)thieno[3,2-*c*]pyridine (10b)

Following the general procedure, **8** (100 mg, 0.39 mmol) in acetonitrile was allowed to react with **2a** (135 mg, 0.47 mmol) in the presence of *p*TSA (3.4 mg, 0.02 mmol) followed by the addition of NH_4OAc (36.6 mg, 0.47 mmol) to afford 5-azabenzothiazole **10b** in 90% yield (171 mg). Brown liquid, R_f = 0.5 (petroleum ether : EtOAc = 8 : 2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.57–7.53 (m, 2H), 7.30 (d, J = 7.4 Hz, 2H), 7.25–7.21 (m, 3H), 7.18–7.11 (m, 6H), 6.99 (d, J = 7.2 Hz, 2H), 4.16 (s, 2H), 4.11 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.1, 147.3, 143.6, 140.2, 138.8, 136.5, 135.0, 132.0, 130.8, 129.4, 128.8, 128.7, 128.6, 128.2, 127.0, 125.9, 122.5, 120.0, 41.0, 37.0; IR (KBr): ν_{max} = 3026, 1488, 1436, 1078, 1011, 749, 699 cm^{-1}; MS (ESI): m/z 470 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{27}H_{21}BrNS$ $(M + H)^+$: 470.0578, found: 470.0560.

UV-visible, emission and lifetime studies

Electronic absorption spectra were recorded using a Shimadzu (model UV-3600) spectrophotometer. Steady-state fluorescence spectra of β-carboline were recorded using a Fluorolog-3 spectrofluorometer (SPEX model, Jobin Yvon) at wavelengths of excitation (λ_{exc}) = 290 and 365 nm. Fluorescence lifetime measurements were measured on a picosecond time correlated single-photon counting (TCSPC) setup (Fluorolog 3-Triple Illuminator, IBH Horiba Jobin Yvon) employing a picosecond light-emitting diode laser (NanoLED, λ_{exc} = 301 nm).

Electrochemical studies

CV experiments were performed on a PC-controlled CH instruments model CHI 620C electrochemical analyzer for β-carboline derivatives in $CHCl_3$ at a scan rate of 200 mV s^{-1} using 0.1 M tetrabutylammonium hexafluorophosphate (Bu_4NPF_6) with glassy carbon, standard calomel electrode and platinum wire as the working, reference and auxiliary electrodes respectively.

Conflicts of interest

There are no conflicts to declare.

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