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Iodine Catalysed Synthesis of Luminescent β-Carboline Tethered Thiazolo[4,5-*c*]carbazole and Naphtho[2,1-*d*]thiazole Derivatives and Estimation of their Light Emitting Properties

Manpreet Singh,[a] Pamita Awasthi,[b] and Virender Singh*[a]

(This manuscript is dedicated to Dr Sanjay Batra on his 55th Birthday)

Abstract: A simple, convenient and highly efficient I_2-catalysed approach has been unfolded towards the synthesis of highly fluorescent β-carboline C-1(3)-tethered thiazolo[4,5-*c*]carbazoles, naphtho[2,1-*d*]thiazoles and benzothiazole derivatives using Kumujian C as a template. This domino strategy proceeds through assembly of 1-formyl-9*H*-β-carbolines, aryl amines and elemental sulfur via formation of one C-N and two C-S bonds in a single operation. Importantly, the methodology was found applicable to β-carboline acetals also. A diversely substituted library of 37 β-carboline tethered arylthiazole hybrids was prepared in excellent yields. The strategy was found appropriate for gram scale synthesis also. The photophysical properties of these fluorophores were also estimated and showed excellent fluorescence properties with quantum yield (Φ_F) up to 92%.

Introduction

The pool of natural products have been an important source of novel chemotypes and bioactive molecules for the development of new drug candidates.[1] Pyrido[3,4-*b*]indole commonly regarded as β–carboline is an important structural motif represented by large number of alkaloids and bioactive compounds (Figure 1) known to exhibit broad spectrum of pharmacological properties including anticancer, antiviral, antibacterial, anti-HIV, antifungal, antimalarial etc.[2] The β-carboline derivatives are specifically known to intercalate into DNA and inhibit the action of topoisomerase I-II, IkK kinase complex, cyclin-dependent kinase and arrest the cell proliferation at various stages which is responsible for their anticancer properties.[3] Abecarnil, Tadalfil and Cipargamin are the few β-carboline based drugs which are used commercially.[4] Recently, the fluorescence properties of β–carboline derivatives have also been explored for the development of novel chemosensors for quantitative detection of fluoride and copper ions at PPB level.[5] The interesting chemical and physical properties of β–carbolines make them a subject of intense research.[6]

Similarly, benzothiazole is another important privileged scaffold[7] which have delivered several drugs being utilized over the years for treating Alzheimer's disease, inflammation, diabetes, tuberculosis and viral infections.[8] In addition to this, benzothiazole derivatives have received considerable attention owing to their impending applications as industrial dyes and organic luminescent materials.[9] Benzothiazole derivatives have also been used as fluorescent probe for imaging live cells.[10]

Attracted by the interesting chemical and physical properties of these two privileged scaffolds, it was envisaged to generate a molecular hybrid of these two frameworks (β-carboline and benzothiazole). In this context, our group used the classical approach toward synthesis of designed prototype via condensation of 1-formyl β-carbolines with 2-aminothiophenoles using ZnO nanoparticles (Figure 2, Eq 4).[11] Interestingly, these benzothiazole derivatives exhibited quantum yield (Φ_F) up to 28%. However, the scope of previous strategy was hampered by the lack of availability of diversely substituted 2-aminothiophenoles derivatives.

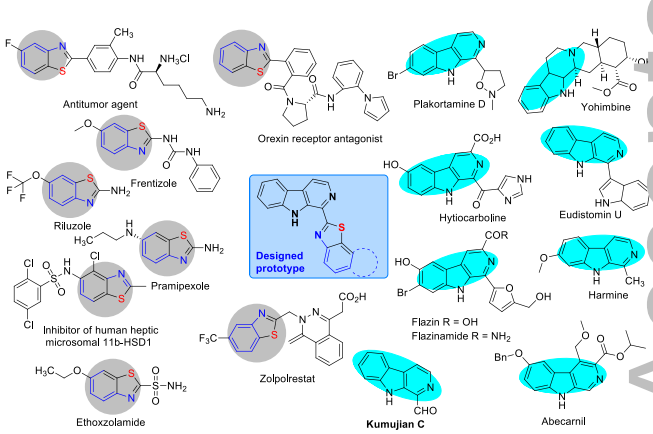

Figure 1. Selected examples of biologically active β-carboline and benzothiazole derivatives

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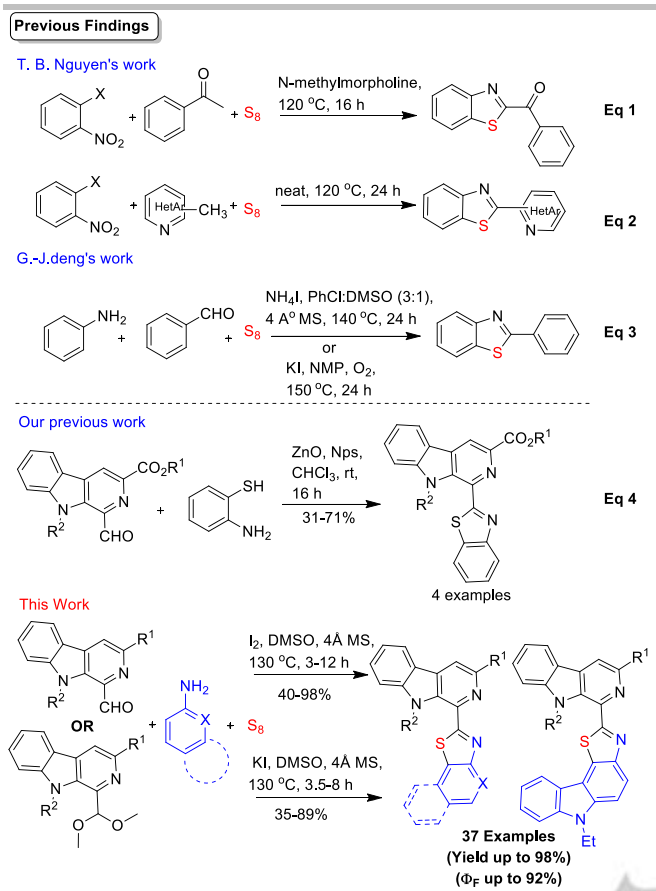
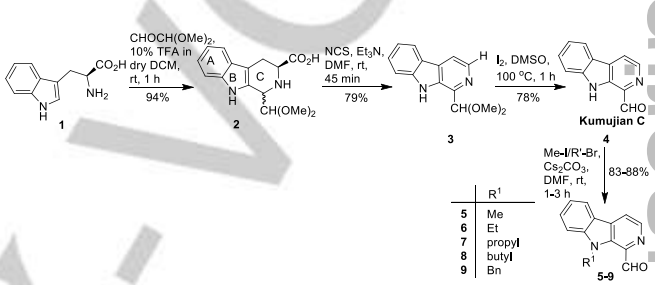


Figure 2. Previous findings related to the synthesis of a designed prototype

The high cost and un-availability of 2-aminothiophenoles have inspired the researchers to develop alternate approaches for the construction of C-S bond. Therefore, various sulfuration agents, such as Belleau's reagent, inorganic metal sulfides, Lawesson's reagent, thioacetates, thiourea and thiocyanates have been explored as the source of sulfur for the generation of C-S bond.[12] The growing environmental concerns have resulted in rise of elemental sulfur as a surrogate option for C-S bond formation. Several research groups[13] have developed many environmentally benign approaches for the construction of C-S bond using elemental sulfur (Figure 2, Eq. 1-3).[14] As a part of our research project towards development of novel β-carboline based molecular hybrids with fluorescent properties using iodine and metal catalysts, we have synthesized β-carboline N-fused imidazoles, oxadiazoles, pyrazoles and lactones.[15] The molecular iodine has attracted substantial attention owing to its less expensive, low-toxicity, readily availability and more versatile nature in contrast to transition-metal catalysts.[16] Therefore, focused efforts were directed toward development of β-carboline C-1(3) tethered thiazole derivatives with extended conjugation to prepare new fluorophores with improved optical properties.[11] With successful synthesis of designed prototypes, the fluorescence properties of these annulated benzothiazole derivatives were also investigated and excellent results were obtained with quantum yield (Φ_F) up to 92%. The results of this detailed study are presented herein.

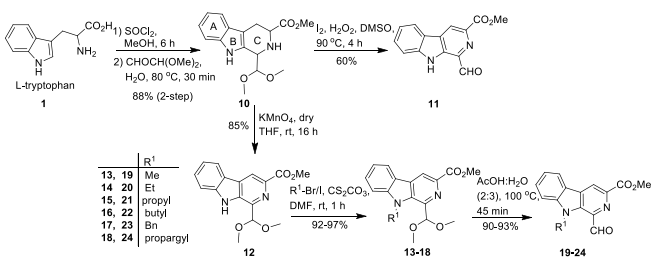
Results and Discussion

The study initiated with the synthesis of β-carboline alkaloid, Kumujian C (**4**) and its derivatives (**5-9**) which were realized via modification in the previous procedure as depicted in Scheme 1.[15] The Pictet-Spengler reaction was performed between L-tryptophan (**1**) and 2,2-dimethoxyacetaldehyde (60% aq. solution) in presence of TFA which afforded the tetrahydro-β-carboline derivative (THβC, **2**) in 94% yield within 1 h. The decarboxylative oxidation of C-ring in THβC derivative **2** with NCS furnished the β-carboline acetal derivative **3** (79%). Further, versatility of I_2 was utilized for the de-protection of acetal **3** to furnish Kumujian C (**4**) in 78% yield.[1e] The *N*-alkyl derivatives of Kumujian C, **5-9** were prepared in 85-88% yield via *N*-alkylation of Kumujian C (**4**) with suitable alkyl halides in presence of Cs_2CO_3 in dry DMF (Scheme 1).



Scheme 1. Synthesis of Kumujian C and *N*-alkyl derivatives

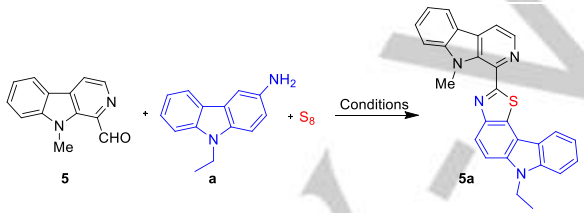
Similarly, other analogues of Kumujian C were prepared in the form of methyl 1-formyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (**11**) and its *N*-alkyl derivatives (**19-24**) from L-tryptophan methyl ester.HCl (generated *in situ* from L-tryptophan) (Scheme 2). The Pictet-Spengler reaction was executed in water at 80 °C which afforded tetrahydro-β-carboline ester derivative (THβC, **10**) in 88% yield within 30 min. The versatility of iodine was again demonstrated for the simultaneous oxidation of THβC **10** as well as *in situ* de-protection of acetal to afford methyl 1-formyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (**11**) by using a combination of iodine with H_2O_2 (30% aq.) in DMSO. To our delight, oxidation of C-ring as well as de-protection of acetal was completed within 4 h to yield the desired product **11** in 60% yields. The *N*-alkyl derivatives of **11** were prepared indirectly *via* selective oxidation of THβC **10** with $KMnO_4$ followed by *N*-alkylation and de-protection of acetal with aqueous AcOH (Scheme 2). Gratifyingly, during the synthesis of *N*-alkyl 1-formyl pyrido[3,4-*b*]indole-3-carboxylate derivatives (**19-24**), purification by column chromatographic was not mandatory at any step and the analytically pure products could be synthesized at gram scale.



Scheme 2. Synthesis of 1-formyl β-carboline derivatives

To achieve the synthesis of targeted prototypes, β-carboline linked arylthiazoles; we set up screening of conditions for the reaction of *N*-methyl Kumujian C, **5** with 3-amino-9-ethylcarbazole (**a**) and elemental sulfur. Initially, model substrate; **5**, 3-amino-9-ethylcarbazole (**a**) and sulfur powder were reacted using I_2 (20 mol%) as a catalyst in dry DMF at 130 °C in presence of 4A° molecular sieves. It was delighting that a clean reaction was obtained and a less polar fluorescent product was isolated in 89% yield (Table 1, entry 1). The analysis of spectroscopic data confirmed the structure of isolated product as β-carboline C-1 tethered thiazolo[4,5-*c*]carbazole derivative **5a**. However, when the same reaction was examined at 100 °C, the yield was reduced to 60% (Table 1, entry 2). It was found that when the reaction was performed in 1,4-dioxane, the desired product was obtained in 71% yield after 12 h (Table 1 entry 3). We further investigated the reaction in THF, DCE and toluene using I_2 as a catalyst but no improvement in yield of desired product was observed (Table 1, entries 4-6). While the reaction was conducted in NMP, 85% yield of desired product **5a** was obtained (Table 1, entry 7). Surprisingly, use of I_2 in ACN resulted in formation of imine only and the reaction failed to yield the desired product even after 24 h (Table 1, entry 8). Therefore, it was considered to explore KI as a catalyst instead of I_2 and a clean reaction with excellent yield (92%) was obtained within 5 h in DMSO at 130 °C (Table 1, entry 9). However, the reaction under similar conditions in dry DMF yielded the desired product **5a** in less quantity (85%, Table 1, entry 10). To our pleasure, when the reaction was executed in DMSO with 20 mol% iodine, the reaction time was reduced to 3.5 h and yield improved to 98% (Table 1, entry 11). At this stage, it was realized that nature of solvent (DMSO) and temperature had a visible impact on the yield of this three component annulation, as it significantly reduced the reaction time and offered the desired product in quantitative amount (98%).

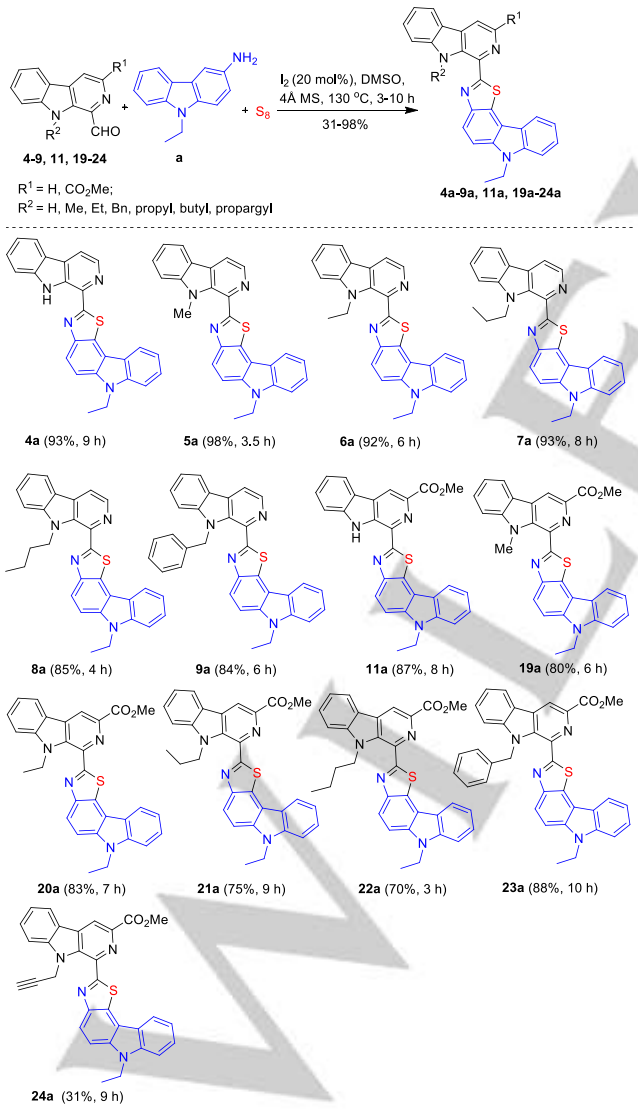
Table 1. Optimisation of reaction conditions[a]



Entry	Catalyst (20 mol%)	Solvent[b]	Temp (°C)	Time (h)	Yields[c] (%)
1	I_2	DMF	130	8.5 h	89%
2	I_2	DMF	100	10 h	60%
3	I_2	1,4-dioxane	130	12 h	71%
4	I_2	THF	130	6 h	77%
5	I_2	DCE	130	7.5 h	60%
6	I_2	toluene	130	12 h	3% (**5a**) + imine
7	I_2	NMP	130	6 h	85%
8	I_2	ACN	80	24 h	imine + **5**
9	KI	DMSO	130	5 h	92%
10	KI	DMF	130	6 h	85%
11	**I_2**	**DMSO**	**130**	**3.5 h**	**98%**
12[d]	I_2	DMSO	130	6.5 h	78%
13	I_2	DMSO	80	11 h	48%
14	I_2	DMSO	100	9 h	70%
15	I_2	DMSO	110	6.5 h	85%
16	I_2	DMSO	140	3.5 h	90%
17[e]	I_2	DMSO	130	5 h	90%
18[f]	I_2	DMSO	130	4 h	94%
19[g]	I_2	DMSO	130	4 h	95%
20[h]	-	DMSO	130	6 h	58%
21[i]	I_2	DMSO	130	8 h	70%

[a] All reactions were performed with 0.95 mmol of **5**, 1.05 mmol of **a** and 4.76 mmol of sulfur powder in presence of 20 mol% of I_2 and 100 mg of 4A° MS in 1.5 mL of anhydrous solvent. [b] Dry solvents were used. [c] Isolated yields of the purified product. [d] 10 mol% of I_2 was used. [e] 2.0 equiv. of sulfur powder was used. [f] 3.0 equiv. of sulfur powder was used. [g] 4.0 equiv. of sulfur powder was used. [h] No catalyst was used. [i] The reaction was performed without 4A° MS.

To investigate the effect of catalyst loading, the reaction was attempted with 10 mol% of iodine, but, a significant decline in the yield (78%) was noted (Table 1, Entry 12). Further, we probed the effect of temperature on the yield and the reaction was performed at 80 °C, 100 °C, 110 °C, 130 °C and 140 °C (Table 1, entries 13-16). A drastic decreased in yield of **5a** was observed (48%) when the reaction temperature was decreased to 80 °C (Table 1, entry 13). As expected, a continuous increase in yield of product (70-85%) was noted with rise in temperature (Table 1, entries 14-15). The yield was optimal at 130 °C (98%) but a further rise in temperature to 140 °C decreased the yield to 90% (Table 1, entries 11, 16). It was also observed that reducing the amount of S_8 from 5 equiv. to 2-4 equiv. had negative impact and yield of the desired product was decreased to 90-95% (Table 1, Entries 17-19). As the reaction progressed with ease in all cases with different catalysts and solvents (except toluene and ACN) to afford the product in good to excellent yields, it was considered worthwhile to investigate the reaction without catalyst. Surprisingly, the reaction yielded the desired product under catalyst-free condition also albeit in low yields (58%, Table 1, entry 20).

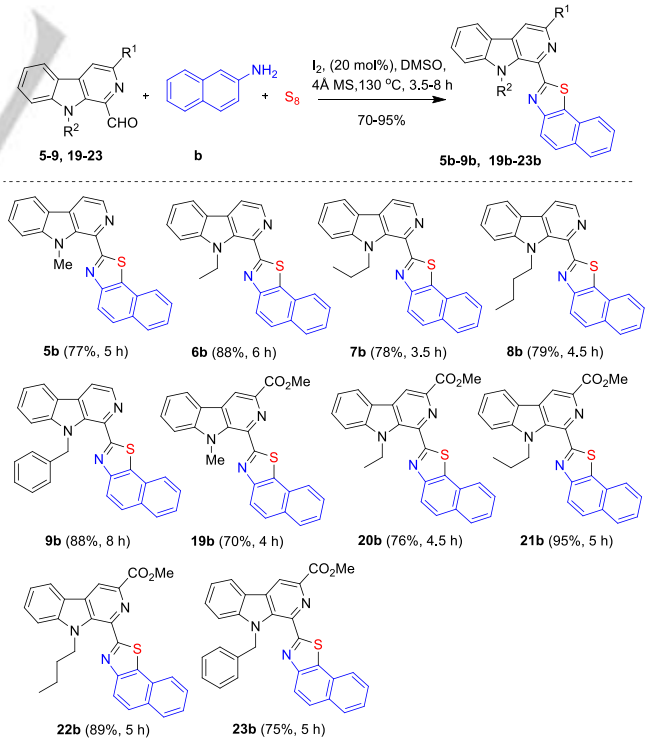


Scheme 3. Iodine catalysed synthesis of β-carboline C-1 tethered thiazolo[4,5-*c*]carbazole derivatives

As all the reactions were performed in presence of molecular sieves (MS), a reaction was examined in the absence of MS and a negative effect on the yield of desired product was noted (Table 1, entry 21) showing the significance of MS. Eventually, the optimization study led to the inference that DMSO was the best solvent and iodine or KI were the suitable catalysts for this desired transformation and 5 equiv. of S_8 with MS were vital for excellent yield of product.

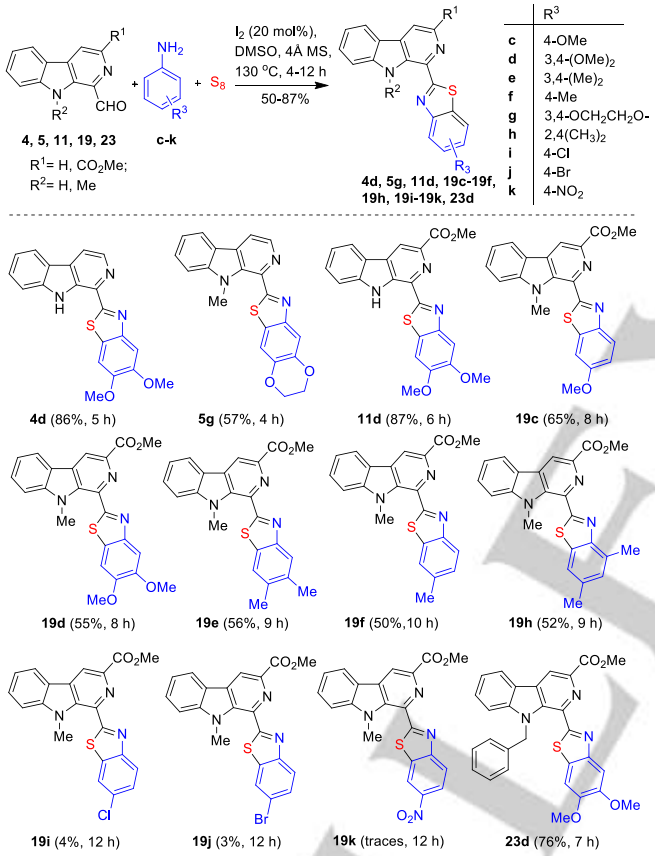
With standardized conditions in hand, the scope of this domino reaction was investigated with Kumujian C (**4**) and its analogues (**5**-**9**, **19**-**24**) with 3-amino-9-ethylcarbazole (**a**) and sulfur powder as depicted in Scheme 3. This strategy was found general in nature and bright fluorescent thiazolo[4,5-*c*]carbazole derivatives (**4a**-**9a**, **19a**-**23a**) were delivered in 70-98% yields within 3-10 h. It is noteworthy to mention that in all cases, a clean reaction was obtained (except **24a**) and only a small column chromatographic purification was necessary just to remove the excess sulfur. 1-Formyl β-carboline bearing *N*-propargyl moiety **24** afforded the desired carbazole annulated thiazole derivative **24a** in poor yield (31%) even after repeated attempts as formation of impurities was observed (Scheme 3).

Next, we sought to extend the scope and generality of this methodology for the preparation of β-carboline C-1 tethered naphtho[2,1-*d*]thiazole derivatives (Scheme 4). Accordingly, the methodology was evaluated with 2-naphthylamine (**b**) for reaction with 1-formyl-9*H*-β-carboline derivatives (**5**-**9**, **19**-**23**). Gratifyingly, under optimized conditions, diversely substituted 1-formyl-9*H*-β-carboline derivatives (**5**-**9**, **19**-**23**) reacted efficiently with 2-naphthylamine (**b**) and elemental sulfur within 3.5-8 h to easily furnish the corresponding 2-(9*H*-pyrido[3,4-*b*]indol-1-yl) naphtho[2,1-*d*]thiazole derivatives (**5b**-**9b**, **19b**-**23b**) in 70-95% yield (Scheme 4).



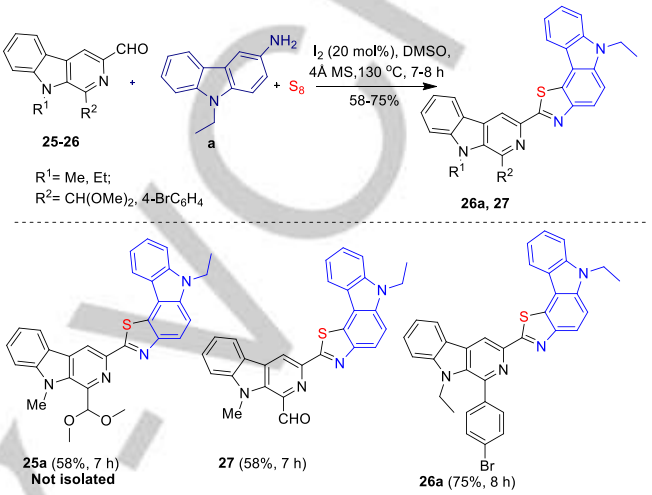
Scheme 4. Synthesis of β-carboline C-1 substituted naphtho[2,1-*d*]thiazole derivatives

Motivated by the successful synthesis of diversely substituted β-carboline C-1 substituted thiazolo[4,5-*c*]carbazoles and naphtho[2,1-*d*]thiazole derivatives, the scope of study was further extended towards construction of β-carboline linked benzothiazoles using substituted anilines **c**-**k** as demonstrated in Scheme 5. The anilines containing electron-donating substituents **c**-**h** responded positively towards this iodine assisted tandem process to furnish the corresponding β-carboline C-1 substituted benzothiazoles (**4d**, **5g**, **11d**, **19c**-**19f**, **19h**, **23d**) in 50-87% yield (Scheme 5). Surprisingly, aniline derivatives **i**-**k** containing electron withdrawing groups such as chloro, bromo and nitro failed to deliver the desired products **19i**-**19k** as the reaction could not proceed beyond imine formation. The desired products **19i**-**19k** were formed in trace amount only under the optimized conditions and could not be isolated from column chromatography even after repeated attempts.



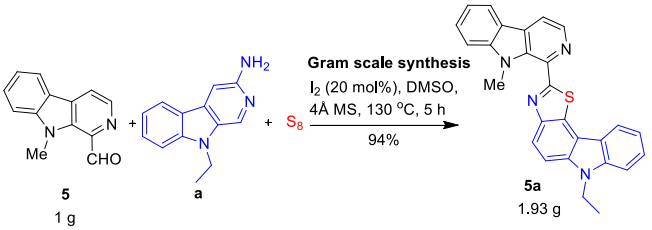
Scheme 5. Synthesis of β-carboline C-1 substituted benzothiazole derivatives

Delighted by the successful synthesis of β-carboline C-1 tethered benzothiazole derivatives from 1-formyl β-carbolines, we investigated the scope of this methodology for the preparation of β-carboline C-3 tethered thiazolo[4,5-*c*]carbazole derivatives from 3-formyl β-carbolines **25**-**26** (Scheme 6).[17] Interestingly, reaction of 1-(dimethoxymethyl)-9-methyl-9*H*-pyrido[3,4-*b*]indole-3-carbaldehyde (**25**) with 3-amino-9-ethylcarbazole (**a**) and elemental sulfur in DMSO in presence of 20 mol% iodine generated a product in 58% yield which was anticipated to be **25a**. However, the spectroscopic analysis of isolated product revealed its structure as 3-(6-ethyl-6*H*-pyrido[3,4-*b*]thiazolo[5,4-*e*]indol-2-yl)-9-methyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde **27** instead of anticipated β-carboline acetal derivatives **25a**. It was inferred that *in situ* de-masking of acetal group in **25a** afforded the product **27**. Moreover, the reaction of 1-(4-bromophenyl)-9-ethyl-9*H*-pyrido[3,4-*b*]indole-3-carbaldehyde (**26**) with 3-amino-9-ethylcarbazole (**a**) and sulfur powder under optimized conditions afforded the expected product **26a** in 75% yield.



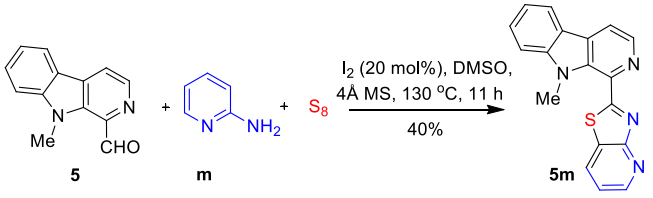
Scheme 6. Synthesis of β-carboline C-3 substituted thiazolo[4,5-*c*]carbazole derivatives

In order to demonstrate the application of present methodology for industrial applications, a gram scale reaction of 9-methyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde (**5**) and 3-amino-9-ethylcarbazole (**a**) with sulfur powder was also performed and to our pleasure, the targeted thiazolo[4,5-*c*]carbazole derivative (**5a**) was obtained in 94% within 5 h after column chromatographic purification (Scheme 7).



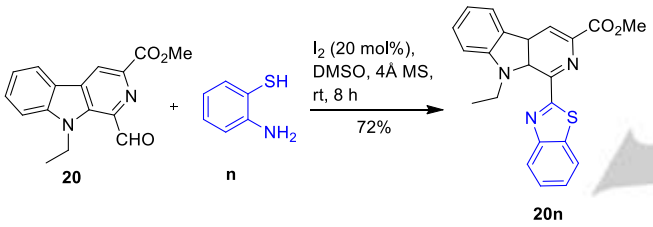
Scheme 7. Gram scale synthesis of β-carboline C-1 tethered thiazolo[4,5-*c*]carbazole

Delighted by these fruitful results, we next turned our attention to broaden the substrate scope of reaction by using 2-aminopyridine (**m**) as the amine component (Scheme 8). Accordingly, the 9-methyl-9*H*- pyrido[3,4-*b*]indole-1-carbaldehyde (**5**) was treated with 2-aminopyridine (**m**) and elemental sulfur under optimized conditions. It was pleasing to find that the anticipated product **5m** was generated in 40% yield under the catalysis of I_2 in DMSO.



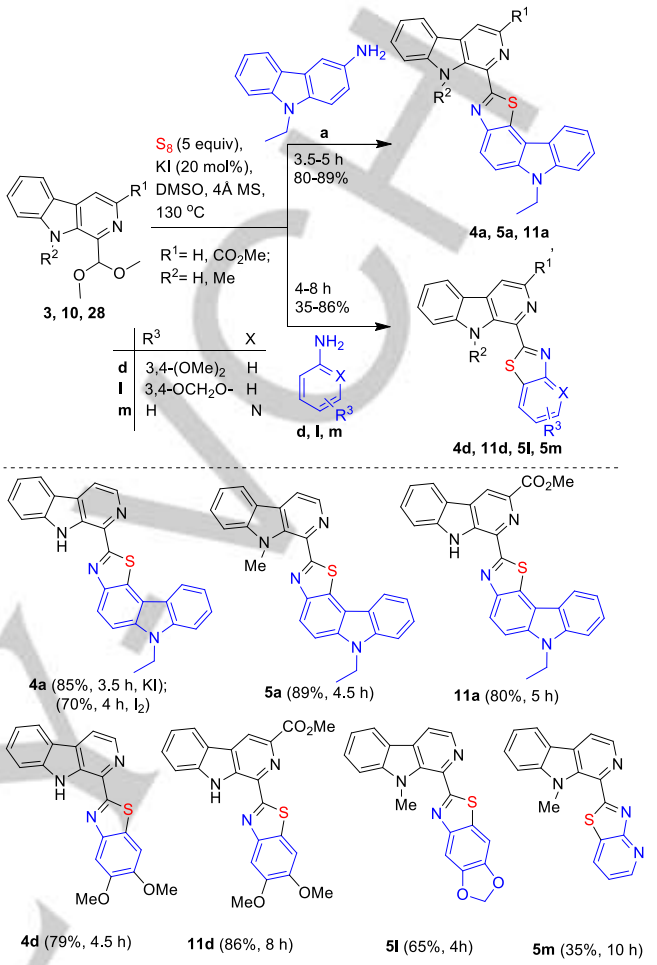
Scheme 8. Synthesis of β-carboline C-1 substituted 2-(9-methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)thiazolo[4,5-*b*]pyridine form 2-aminopyridine

Furthermore, the catalytic property of I_2 in DMSO was demonstrated for the conventional condensation of 2-aminothiophenol (**n**) containing pre-installed thiol moiety with methyl 9-ethyl-1-formyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (**20**) at room temperature (Scheme 9).[11] Interestingly, the desired product, β-carboline C-1 substituted benzothiazole derivative **20n** was achieved in 72% yields. The reaction under heating condition at 130 °C completed in less time (4.5 h) but yielded the desired product in 52% yield as impurities were generated under heating condition.



Scheme 9. Classical approach towards I_2 catalysed synthesis of β-carboline C-1 substituted benzothiazole derivative form 2-aminothiophenol

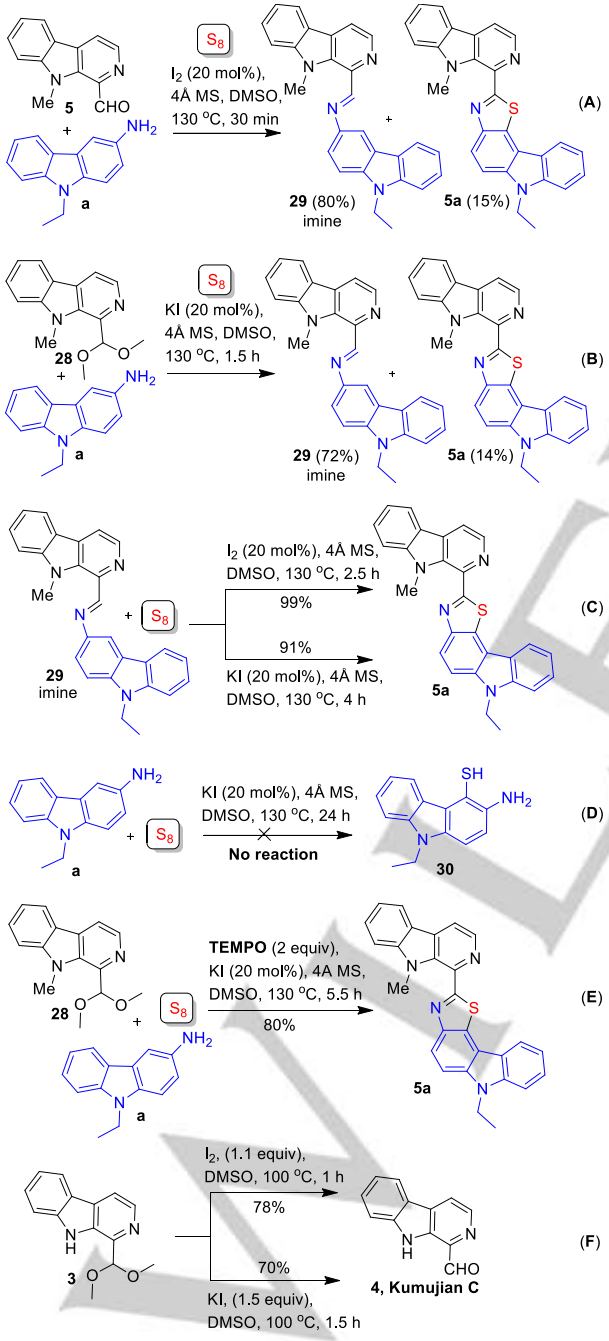
During the synthesis of **25a** (**27**) in Scheme 6, it was realized that under optimum conditions, the de-protection of acetal functionality occurred. Therefore, it was considered worthwhile to take advantage of this observation and investigate the scope of present strategy for the synthesis of benzothiazoles from aromatic acetals instead of aldehydes. Accordingly, 1-(dimethoxymethyl)-9*H*-pyrido[3,4-*b*]indole (**3**, **10** and **28**) containing acetal moiety at C-1 position were employed as substrate for reaction with 3-amino-9-ethylcarbazole (**a**) and S_8 instead of aldehyde as it may reduce one step in the synthesis of proposed prototypes. Alternatively, it may open up avenues for the synthesis of benzothiazole derivatives from acetals where aldehydes are unstable. It was noticed that the reaction of acetal **3** under optimized condition in I_2 gave the desired product identical to **4a** in 70% yield in 4 h. But, when the same reaction was performed under the catalysis of KI (20 mol%) instead of I_2, then respective product **4a** was isolated in much better yield (85%) in less time (3.5 h). Similarly, **5a** and **11a** were obtained in 80-89% yields. Therefore, KI turned out be a better catalyst than I_2 for synthesis of desired prototypes from acetals. Further, we investigated the scope of this alternate approach with anilines and 2-aminopyridine (**d**, **l** and **m**). To our pleasure, electron donating anilines as well as 2-aminopyridine reacted readily in presence of KI in DMSO to generate the anticipated β-carboline tethered benzothiazole derivatives (**4d**, **11d**, **5l**, **5m**) in 35-86% yield as depicted in Scheme 10.



Scheme 10. Synthesis of β-carboline C-1 linked benzothiazoles form acetal derivatives

To probe the mechanistic route of this reaction, some control experiments (**A-F**) were conducted as presented in Scheme 11. The reaction of *N*-methyl Kumujian C (**5**) was carried out with 3-amino-9-ethylcarbazole (**a**) and S_8 in presence of I_2 in DMSO at 130 °C but the reaction was quenched after 30 min. A column chromatographic purification of reaction mixture yielded the imine intermediate **29** (80%, analyzed by spectroscopy) and β-carboline C-1 tethered thiazolo[4,5-*c*]carbazole **5a** (15%). Similarly, a reaction of **28** with 3-amino-9-ethylcarbazole (**a**) and S_8 in presence of KI in DMSO in 1.5 h generated the imine intermediate **29** (72%) and anticipated product **5a** (14%) (Scheme 11, **A**-**B**). This isolated imine intermediate **29** was again reacted with elemental sulfur in presence of I_2 as well as KI in DMSO which smoothly yielded the desired product **5a** in 99% and 91% yields respectively (Scheme 11, **C**). These results clearly indicated that reaction proceeds through formation of imine intermediate followed by sulfur insertion. Next, we speculated that 3-amino-9-ethyl-9*H*-carbazole-4-thiol (**30**) may be formed a key intermediate before cyclisation with **5**, (thought appeared from Scheme 9) therefore we performed another controlled experiment (**D**) in the absence of **5** to understand the reaction mechanism, but 3-amino-9-ethylcarbazole did not

convert into thiol derivative **30** (Scheme 11, **D**). In another control experiment (**E**), the reaction was performed in presence of radical scavenger (2.0 equiv. TEMPO), however, the reaction proceeded smoothly to afford desired product **5a** in 80% yield (Scheme 11, **E**) which ruled out the possibility of a free radicals mechanism. It was also found that the acetal de-protection can be effected with both I_2 as well as KI in DMSO under heating conditions at 100 °C (Scheme 11, **F**). However, during the synthesis of arylthiazole derivatives from acetals with KI (Scheme 10), it was observed that free aldehyde was not detected in reaction mixture at any interval of time and either acetal or imine or final product was detected (Although acetal could be de-protected with KI, **F**).



Scheme 11. Control experiments

Based on results of controlled experiments and previous findings[13] a reasonable mechanism for the formation of β-carboline C-1(3) tethered thiazolo[4,5-*c*]carbazoles, naphtho[2,1-*d*]thiazoles and benzothiazole derivatives is depicted in Figure 3. The reaction proceeds with the formation of imine intermediate **29** by condensation of 1-formyl β-carboline **5** or acetal **28** and 3-amino-9-ethyl-9*H*-carbazole (**a**) in presence of I_2 or KI in DMSO. Further N-iodination of imine **29** may lead to the generation of iodonium intermediate **30**. Now the reaction may follow two different possible pathways (Figure 3). The electrophilic attack of sulfur at the electron rich *ortho* position of amine in aromatic ring (carbazole) may proceed through the path 1, where elimination of S_7 may result in formation of sulfurated imine intermediate **32**. The desired product **5a** may be formed through intramolecular cyclization of **32** followed by oxidative aromatization of **33** which may be assisted by the presence of sulfur (Figure 3). Alternatively, the reaction may follow path 2 where the nucleophilic addition of sulfur at the imine carbon may generate intermediate **34**. The subsequent intramolecular electrophilic addition of sulfur on the aromatic ring of amine may lead to the formation of cyclic intermediate **35**. The deprotonation of **35** may lead to dihydrothiazolo[4,5-*c*]carbazole derivative **36** which after oxidation may yield final product **5a**. It seems that reaction favors the path 1 and evidence appears from Scheme 5, where it was observed that the reaction with anilines bearing electron withdrawing substituents failed to generate the desired benzothiazole derivatives.

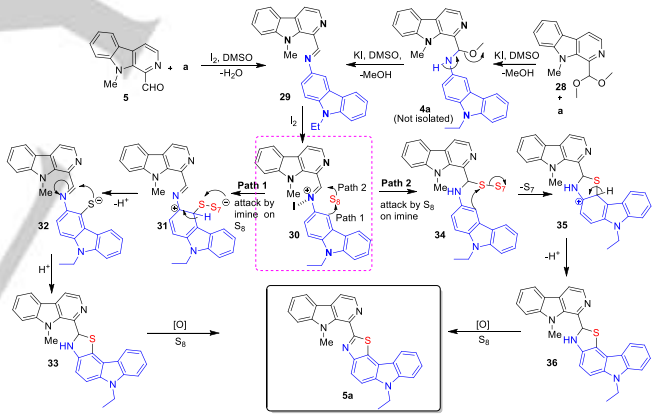


Figure 3. Proposed mechanism for the formation of β-carboline C-1 tethered thiazolo[4,5-c]carbazole derivative

Photophysical Studies

The benzothiazole derivatives have emerged as excellent fluorophores owing to their luminescent properties,[9-10] therefore, light emitting properties of β-carboline C-1(3) tethered thiazolo[4,5-*c*]carbazole, naphtho[2,1-*d*]thiazole and benzothiazole derivatives were analyzed. The fluorescence quantum yield (Φ_F) of these β-carboline tethered arylthiazole derivatives was calculated relative to quinine sulphate (Φ_R = 0.546 in 0.1 M H_2SO_4 at 350 nm) as a standard fluorophore. The brightness of these newly generated fluorophores was measured by multiplication of quantum yield (Φ) with their molar extinction coefficient (ε). In order to measure the UV-Vis absorption and fluorescence emission of samples, stock solutions of 1.0 mM concentration were prepared and diluted to

5.0 μM concentration using DCM as the solvent. The quantum yields were calculated as per the equation:

$$\Phi_S = \Phi_R \times \frac{I_S}{I_R} \times \frac{A_R}{A_S} \times \frac{\eta_S^2}{\eta_R^2}$$

$$R - \text{Reference}\,;\, S - \text{Sample}$$

In order to achieve maximum emission, the optimization of solvents was carried out by using β-carboline C-1 tethered thiazolo[4,5-*c*]carbazole **21a** as the model substrate (Figure 4). It was observed that the synthesized products were readily soluble in DCM, DMSO, THF and ACN but moderately soluble in MeOH. The thiazolo[4,5-*c*]carbazole derivative **21a** exhibited significant fluorescence emission in DCM, THF, DMSO as well as ACN but the maximum fluorescence emission was obtained in DCM (Figure 5). Expectedly, the maximum quantum yield (*Φ*) was produced in DCM (52%) as illustrated in Table 2. We also calculated the Stokes shits, molar extinction coefficient as well as brightness for compound **21a** in different solvent (Table 2). As the best results were obtained in DCM, therefore, the photophysical properties of all other synthesised compounds were analysed in DCM as a solvent.

Table 2. Optimisation of solvents for analysis of photophysical properties of β-carboline C-1 tethered thiazolo[4,5-*c*]carbazole[a]

Solvents **21a**	UV-Vis	Fluorescence		Molar Extinction Coeff. (ε) ($M^{-1}cm^{-1}$)	Brightness	Stokes shift (nm)	Quantum Yield[b] Φ_F
	λ_{Ex} (nm)	λ_{Em} (nm)	Intensity (a.u.)				
THF	296	465	692.63	62000	18600	169	0.30
DCM	**299**	**467**	**762.13**	**49600**	**25584**	**168**	**0.52**
DMSO	296	478	452.13	56400	18048	183	0.32
ACN	299	469	652.25	40600	15428	170	0.38

[a] The Photophysical properties were measured at 5 μM concentration. [b] The quantum yields (Φ_F) were calculated relative to quinine sulfate as a reference.

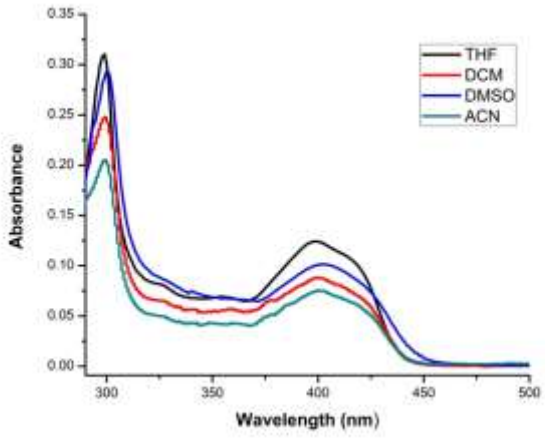


Figure 4. UV-Visible spectra of compound **21a** in THF, DCM, DMSO and ACN at 5 μM concentration

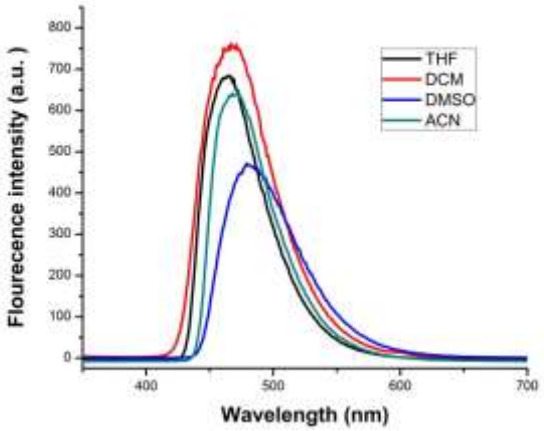


Figure 5. Fluorescence spectra of compound **21a** in THF, DCM, DMSO and ACN at 5 μM concentration

It is worthwhile to mention that we have analysed the fluorescence spectra of most of the β-carboline derivatives at two or three excitation wavelengths as presented in Table 3-5 and also calculated the corresponding luminescence quantum yields. Initially, the photophysical properties of β-carboline C-1 tethered thiazolo[4,5-*c*]carbazole derivatives (**4a-9a**, **11a**, **19a-23a** and **26a**) were evaluated in DCM. It was realized that the carbon length of R^2 substituents at *N*-9 position and H/ester functionality at C-3 position had clear impact on the emission maxima and quantum yield of these compounds (**4a-9a**, **11a**, **19a-23a** and **26a**). The red shift was observed in emission maxima of **4a**-**9a** (except **8a**) excited at 290-299 nm (Figure 6) with increase in length of carbon chain at *N*-9 position. The fluorophore, **4a**-**9a** displayed strong fluorescence intensity and quantum yield (Φ_F up to 92%). Similarly, bathochromic shift was observed in emission maxima of **19a**-**23a** excited at 297-298 nm with lengthening of carbon chain at *N*-9 position as depicted in Table 3. The β-carboline C-1 tethered thiazolo[4,5-*c*]carbazole derivatives **4a**-**9a** exhibited higher fluorescence intensity (Figures 6-7) and quantum yield (Table 3) as compared to similar analogues bearing ester moiety at C-3 position, though a regular trend was not present. In this series, the propyl chain at N-9 position was optimum for excellent quantum yield (**7a**, Φ_F 92% and **21a**, Φ_F 82%). In short, all the β-carboline C-1(3) tethered thiazolo[4,5-*c*]carbazole derivatives showed excellent photophysical properties with quantum yield (Φ_F) ranging from 26 to 92 %. These β-carboline derivatives (**4a**-**9a**, **11a**, **19a**-**23a** and **26a**) exhibited maximum molar extinction coefficient of 132600 ($M^{-1}Cm^{-1}$) with highest brightness up to 37468 as presented in Table 3.

Table 3. Photophysical properties of β-carboline C-1(3) tethered thiazolo[4,5-*c*]carbazole derivatives[a]

Compound No.	UV-Vis	Fluorescence		Molar Extinction Coeff. (ε) ($M^{-1}cm^{-1}$)	Brightness	Stokes shift (nm)	Quantum Yield[b] Φ_F
	λ_{Ex} (nm)	λ_{Em} (nm)	Intensity (a.u.)				

4a	297 397 414	458 469 456	200.97 163.52 190.65	21000 13000 14800	6930 5330 6068	161 65 42	0.33 0.41 0.41
5a	290 399	464 463	640.90 354.65	37600 16200	21432 11826	174 64	0.57 0.73
6a	299 400	465 465	999.00 947.33	132600 55600	37128 31692	166 65	0.28 0.57
7a	299 350 400	466 465 465	998.00 659.07 962.57	129200 26000 54000	37468 23920 31320	167 115 65	0.29 0.92 0.58
8a	299 400	463 466	996.04 919.20	124200 51800	37260 30044	164 66	0.30 0.58
9a	299 399	466 465	815.15 464.84	49200 22000	27552 16280	167 66	0.56 0.74
11a	297 418	472 465	86.84 27.21	8200 5000	3936 1150	175 47	0.48 0.23
19a	298 400	466 465	998.00 785.87	122000 45400	36600 26786	168 65	0.30 0.59
20a	299 399	467 468	755.89 393.61	53200 19800	26068 13266	168 69	0.49 0.67
21a	299 399	467 468	762.13 391.60	49600 16200	25584 13284	168 69	0.52 0.82
22a	299 400	468 468	695.77 347.03	41000 14800	23780 11544	169 68	0.58 0.78
23a	299 399	471 459	806.81 440.35	54400 21800	27744 15042	172 60	0.51 0.69
26a	297 372	429 430	304.73 332.65	39000 35400	10140 10620	132 58	0.26 0.30

[a] The photophysical properties were measured at 5 μM concentration. [b] The quantum yields (Φ_F) were calculated relative to quinine sulfate as a standard.

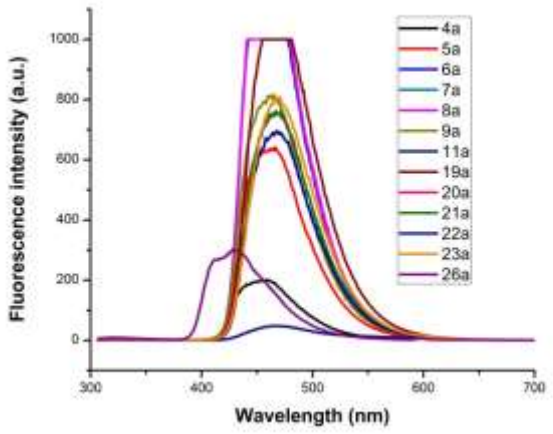


Figure 6. Fluorescence spectra of β-carboline C-1(3) tethered thiazolo[4,5-*c*]carbazole derivatives excited (λ_{Ex}) at 290–299 nm

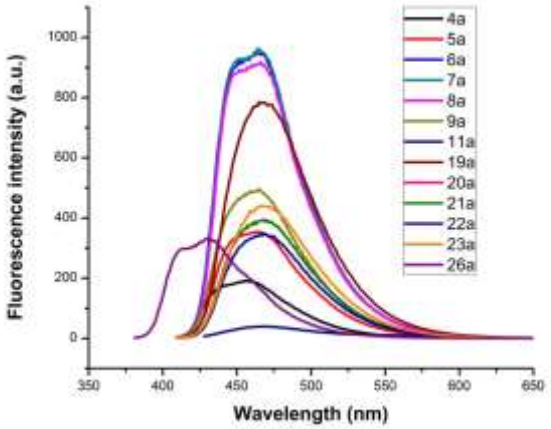


Figure 7. Fluorescence spectra of β-carboline C-1(3) tethered thiazolo[4,5-*c*]carbazole derivatives excited (λ_{Ex}) at 372–418 nm

In the case of β-carboline C-1 substituted naphtho[2,1-*d*]thiazole derivatives (**5b**-**9b**, **19b**, **21b**, **22b**); the compounds **5b**-**8b** excited at 395-396 nm (Figure 9) surprisingly exhibited hypsochromic shift (Blue-shift) in 460-443 nm emission wavelength with lengthening of aliphatic chain at N-9 position of β-carboline ring i.e. methyl < ethyl < n-propyl < n-butyl at the N-9 position as presented in Table 4 and Figure 9. However, the compounds **19b**, **21b** and **22b** showed bathochromic shift (red-shift) in emission wavelength at 457-462 nm when excited at 286-288 nm (Figure 8) with increase in length of aliphatic chain at N-9 position i.e. methyl < n-propyl < n-butyl. In this series also, the propyl chain at N-9 position was optimum for excellent quantum yield (**7b**, Φ_F 26% and **21b**, Φ_F 31%) as shown in Table 4. The β-carboline linked naphtho[2,1-*d*]thiazole derivatives displayed good quantum yield ranging from 12 to 31% which was significantly less than corresponding thiazolo[4,5-*c*]carbazole analogues (26-92 %).

Table 4. Photophysical properties of β-carboline C-1 tethered naphtho[2,1-*d*]thiazole derivatives[a].

Compound No.	UV-Vis	Fluorescence		Molar Extinction Coeff. (ε) ($M^{-1}cm^{-1}$)	Brightness	Stokes shift (nm)	Quantum Yield[b] Φ_F
	λ_{Ex} (nm)	λ_{Em} (nm)	Intensity (a.u.)				
5b	289 395	452 460	105.70 61.96	28800 16800	4032 2016	163 65	0.14 0.12
6b	288 396	461 458	109.21 64.51	21800 9400	3924 2068	176 62	0.18 0.22
7b	290 399	445 450	179.78 103.55	28000 13000	6160 3380	155 51	0.22 **0.26**
8b	299 399	446 443	212.90 77.90	37000 17800	7030 2492	147 44	0.19 0.14
9b	289 394	452 455	261.06 180.85	65000 32000	8450 5760	163 61	0.13 0.18
19b	286 395	457 458	258.91 163.96	98400 37600	8856 5264	171 63	0.09 0.14
21b	287 399	460 451	65.60 27.21	8600 3200	2666 960	173 52	**0.31** 0.30

22b	288 399	462 461	236.59 116.93	43000 16000	8170 3840	174 62	0.19 0.24

[a] The photophysical properties were measured at 5 μM concentration. [b] The quantum yields (Φ_F) were calculated relative to quinine sulfate (0.1 M aq. H_2SO_4, excited at 350 nm) as a reference.

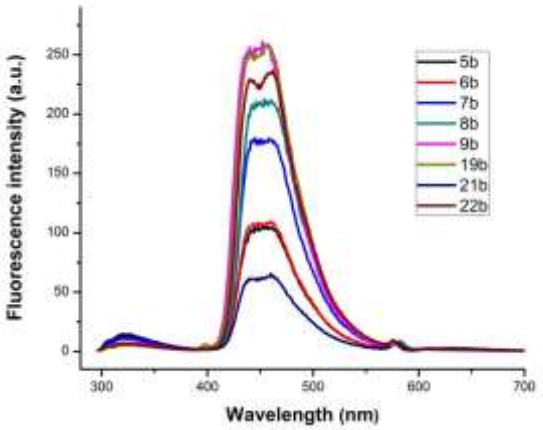


Figure 8. Fluorescence spectra of β-carboline C-1 tethered naphtho[2,1-*d*]thiazole derivatives excited (λ_{Ex}) at 286–299 nm

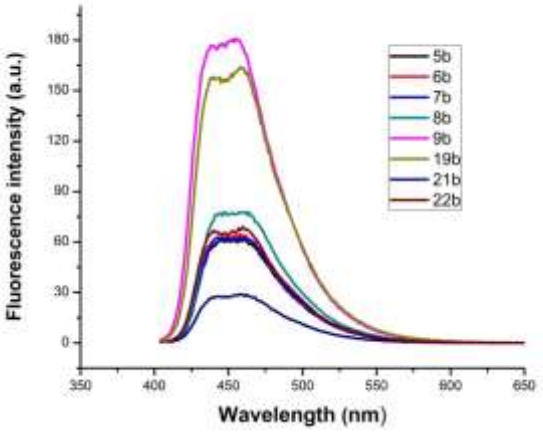


Figure 9. Fluorescence spectra of β-carboline C-1 tethered naphtho[2,1-*d*]thiazole derivatives excited (λ_{Ex}) at 394–399 nm

The emission maxima of β-carboline substituted benzothiazole derivatives (afforded from anilines) **11d**, **19c**, **5g**, **19f**, **23d** showed bathochromic shift when excited at 277-302 nm (Figure 10) with variation in substituents (H, Me and benzyl) at *N*-9 position of β-carboline ring and obtained emission ranging from 448 to 461 nm. Considering the regioisomeric effects of specific auxochromes such as methoxy and methyl groups in the benzothiazole ring, the fluorophore **19c**, **19f** and **23d** showed excellent fluorescence quantum yields (36-68%) while **11d** devoid of substitution at *N*-9 position in β-carboline ring showed low quantum yield (10%) in this series as shown in Table 5. The maximum molar extinction coefficient for these β-carboline C-1 tethered benzothiazole derivatives (**11d**, **19c**, **5g**, **19f** and **23d**) was found to be 74000 $mol^{-1}cm^{-1}$ for **19f** while highest stokes shift was 182 nm (Table 5 and Figure 11). Interestingly, the thiazolo[4,5-*b*]pyridine derivative **5m** afforded from 2-aminopyridine showed single absorption and excitation maxima and exhibited 15% quantum yield (Table 5). In summary, the β-carboline C-1(3) tethered thiazolo[4,5-*c*]carbazole, naphtho[2,1-*d*]thiazole and benzothiazole derivatives showed a wide region of fluorescence emissions (λ_{Em}, 428–470 nm) along with excellent quantum yields (up to 92%). The thiazolo[4,5-*c*]carbazole derivatives displayed maximum quantum yield (26-92%) followed by benzothiazoles (Φ_F = 8-68%) and then naphtho[2,1-*d*]thiazole derivatives (Φ_F = 12-31%).

Table 5. Photophysical properties of β-carboline C-1 tethered benzothiazole derivatives[a]

Compound No.	UV-Vis	Fluorescence		Molar Extinction Coeff. (ε) ($M^{-1}cm^{-1}$)	Brightness	Stokes shift (nm)	Quantum Yield[b] Φ_F
	λ_{Ex} (nm)	λ_{Em} (nm)	Intensity (a.u.)				
5g	302 374	457 459	13.19 7.91	9000 3400	810 374	155 85	0.09 0.11
11d	277 407 388	448 447 447	136.74 148.33 139.11	6000 52800 44600	480 4752 4460	171 40 59	0.08 0.09 0.10
19c	280 318 387	449 444 446	291.76 258.91 181.59	34600 25400 16400	9688 8382 5904	169 126 59	0.28 0.33 0.36
19f	279 394	457 462	757.29 540.87	74000 37200	25900 17856	178 68	0.35 0.48
23d	279 392	461 463	431.14 281.17	30200 14200	15100 9656	182 71	0.50 0.68
5m	301	459	36.28	12400	1860	158	0.15
20n	287 385	441 443	197.99 118.67	52600 19800	6312 3762	154 59	0.12 0.19

[a] The photophysical properties were measured at 5 μM concentration. [b] The quantum yields (Φ_F) were calculated relative to quinine sulfate (0.1 M aq. H_2SO_4, excited at 350 nm) as a reference.

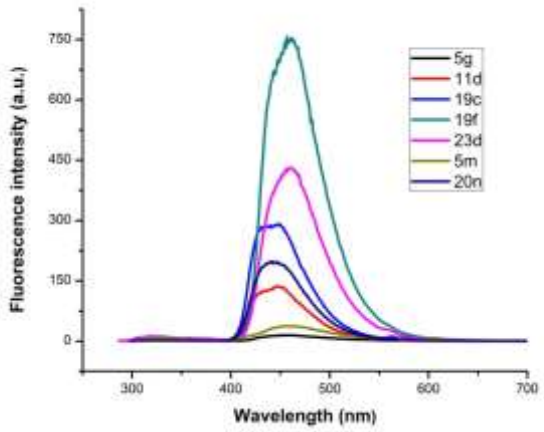


Figure 10. Fluorescence spectra of β-carboline C-1 substituted benzothiazole derivatives excited (λ_{Ex}) at 277–302 nm

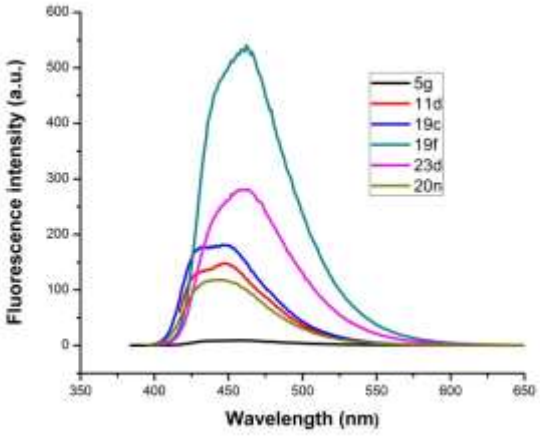


Figure 11. Fluorescence spectra of β-carboline C-1 substituted benzothiazole derivatives excited (λ_{Ex}) at 374–407 nm

Conclusions

In conclusion, a simple and highly efficient I_2-catalysed oxidative annulation strategy has been developed for the first time for the synthesis of β-carboline C-1(3) tethered benzothiazoles, naphtho[2,1-d]thiazoles and thiazolo[4,5-c]carbazoles via three component assembly of Kumujian C (1-formyl 9*H* β-carbolines), 3-aminocarbazole/anilines/2-aminopyridine/naphthylamine and elemental sulfur. Importantly, the strategy was applicable to acetal derivatives also and could be used where aldehydes are not stable. This modular approach could produce the products in excellent yields with ease which makes the methodology highly efficient and practical for the preparation of this class of compounds. Furthermore, this efficient and operationally simple protocol features use of non-toxic and inexpensive catalyst (I_2/KI) and the strategy is amenable to gram scale synthesis. Moreover, light emitting properties of the synthesized compounds were also investigated and these molecular hybrids emerged as excellent fluorophores with quantum yield (Φ_F) up to 92%. The thiazolo[4,5-*c*]carbazole derivatives displayed maximum quantum yield (26-92%) followed by benzothiazoles (Φ_F = 8-68%) and then naphtho[2,1-*d*]thiazole derivatives (Φ_F = 12-31%.

Experimental Section

All Chemicals and reagents were purchased from Sigma Aldrich, Acros, Spectrochem Ltd. and Avera Synthesis and used without further purification. Commercially available anhydrous solvents (DMSO, THF, MeOH, toluene, ACN, diethylether and DMF) were used as received without further distillation. Thin layer chromatography (TLC) was performed on precoated aluminum plates (E. Merck; silica gel 60 PF254, 0.25 mm). Column chromatography was performed on silica gel (SRL; 60–120 mesh). Melting points were determined in open-ended capillary tubes on a Precision Digital melting-point apparatus (LABCO) that contained silicon oil and are uncorrected. IR spectra were recorded on an Agilent FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on an Avance III Bruker spectrometer at operating frequencies of 400 MHz, 500 MHz (^{1}H) or 100 MHz, 125 MHz (^{13}C), as shown in the individual spectrum, by using tetramethylsilane (TMS) as an internal standard. HRMS spectra were recorded on 6200 series TOF/6500 series QTOF B.05.01 (B5125). Room temperature varied between 25–40 °C. The multiplicity in the ^{1}H NMR spectra is as follows: s for singlet, d for doublet, t for triplet, q for quartet, dd for doublet of doublet and m for multiplet.

General procedure for preparation of Kumujian C (9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde, **4**).To a stirred solution of 1-(dimethoxymethyl)-9*H*-pyrido[3,4-*b*]indole (**3**; 2 g, 8.26 mmol) in dry DMSO (15 mL); I_2 (2.30 g, 9.08 mmol) was added and the reaction mixture was stirred for 1 h at 100 °C. After completion of reaction, as monitored by TLC, the content was cooled to room temperature and quenched with 10% aqueous solution of sodium thiosulfate. Thereafter, reaction content was poured into ice cold water (50 mL) under stirring which resulted in formation of yellow precipitates. These precipitates were filtered through Buckner funnel and dried in air under suction. the product was further triturated and washed with diethyl ether to yield analytically pure product as yellow solid, **4** (1.26 g, 78%; R_f = 0.49 (hexane/EtOAc, 70: 30, v/v).

General procedure for preparation of *N*-alkyl derivatives of Kumujian C (**4**-**9**) **as exemplified for 9-methyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde** (**5**). To a stirred solution of Kumujian C (**4**; 1.00 g, 5.1 mmol) in dry DMF (30 mL), CS_2CO_3 (2.9 g, 9.18 mmol) was added and stirred the reaction mixture at room temperature for 10 min. Thereafter, methyl iodide (0.38 mL, 6.12 mmol) was added drop-wise and the reaction mixture was stirred for additional 1 h at room temperature. On completion of the reaction, as monitored by TLC, the content was poured into ice cold water (40 mL) under stirring which resulted in formation of yellow precipitates. The precipitates were filtered through Buckner funnel and dried in air under vacuum. The precipitates were triturated and washed twice with cold ether to get yellow solid product, **5** (0.95 g, 88%; R_f = 0.65 (hexane/EtOAc, 70:30, v/v).

General procedure for the preparation of methyl 1-formyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (**11**). To a stirred solution of methyl 1-(dimethoxymethyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-*b*]indole-3-carboxylate (**10**; 5g, 16.4 mmol) in DMSO at room temperature, H_2O_2 (2.4 mL, 98.6 mmol, 6 equiv., 30% aq.) and I_2 (0.835 g, 3.39 mmol) were added. The reaction temperature was then slowly raised to 100 °C and stirred for 4 h. After completion of the reaction as revealed by TLC, the reaction mixture was cooled to room temperature and quenched with sodium thiosulfate (50 mL, 10% aqueous solution) under stirring which resulted in formation of yellow precipitates. The reaction mass was filtered through the Buckner funnel and dried in air which was further purified by column chromatography on silica gel (EtOAc/-hexane 15:85, v/v) to obtain the pure product as a yellow solid, **11** (2.5 g, 60% yield; R_f = 0.47 (hexane/EtOAc, 70:30, v/v). It was noted that after mixing of **10** with H_2O_2 and I_2; a solid reaction mass is formed at room temperature under stirring which should be heated at 100 °C for 4 h but reaction temperature should be raised slowly to 100 °C as reaction was observed to exothermic in nature.

General procedure for the preparation of 3a-9a, 11a, 19a-24a, 26a, 27 5b-9b, 19b-23b 4d, 5g, 11d, 19c-19f, 19h-19k, 23d and 5m as exemplified for 6-ethyl-2-(9-methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-6*H*-thiazolo[4,5-*c*]carbazole (**5a**)**.** To a stirred solution of 9-methyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde (**5**; 0.20 g, 0.95 mmol) in anhydrous DMSO (1.5 mL); 3-amino-9-ethylcarbazole (a; 0.220 g, 1.05 mmol), S_8 (0.152 g, 4.76 mmol), I_2 (20 mol %, 0.048 g) and 4Å molecular sieves (100 mg) were added and reaction content was heated at 130 °C for 3.5 h. On completion of the reaction, as confirmed by TLC, the reaction content was cooled to room temperature and quenched with sodium thiosulfate (10% aqueous solution). Thereafter, reaction mixture was poured into ice cold water (30 mL) under stirring which resulted in formation of yellow precipitates. The precipitates were filtered through Buckner funnel under vacuum. The product was further purified by a short silica-gel (60-120 mesh) column chromatography using EtOAc/hexane (10:90, v/v) as an eluent to obtain the pure product as a yellow solid, **5a** (0.405 g, 98%; R_f = 0.78 (hexane/EtOAc, 70:30, v/v). It is

mentioned that in all cases, a clean reaction was obtained (except **24a**) and column chromatographic purification was required to remove excess sulfur only. All the products had good solubility and were easily eluted using EtOAc: Hexane (10:90, v/v).

Gram scale synthesis of 6-ethyl-2-(9-methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-6*H*-thiazolo[4,5-*c*]carbazole (5a). A 50 mL round bottom flask was charged with 9-methyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde (**5**; 1 g, 4.76 mmol), 3-amino-9-ethylcarbazole (**a**; 1.1 g, 5.24 mmol), S_8 (0.761 g, 23.8 mmol), I_2 (20 mol %, 0.241 g), 4Å MS (400 mg), DMSO (10 mL) and were heated at 130 °C for 5 h. On completion of the reaction, as monitored by TLC, reaction content was cooled to room temperature and quenched with sodium thiosulfate (10% aqueous solution). Thereafter, the reaction content was poured into crushed ice/ice cold water (70 mL) under stirring which resulted in formation of precipitates. The solid mass was filtered through Buckner funnel to get the product. Which was further purified by column chromatography on silica gel using (EtOAc/hexane 10:90, v/v) as an eluent to obtain the pure product as a yellow solid, **5a** (1.93 g, 94% yield; R_f = 0.78 (hexane/EtOAc, 70:30, v/v).

General procedure for the preparation of 4a, 5a, 11a, 4d, 11d, 5l and 5m as exemplified for 6-ethyl-2-(9*H*-pyrido[3,4-*b*]indol-1-yl)-6H-thiazolo[4,5-*c*]carbazole (**4a**). To a stirred the solution of 1-(dimethoxymethyl)-9*H*-pyrido[3,4-*b*]indole (**3**; 0.200 g, 0.83 mmol) in DMSO (1.5 mL); 3-amino-9-ethylcarbazole (a; 0.190 g, 0.91 mmol), S_8 (0.132 g, 4.13 mmol), KI (0.027 g, 20 mol%), and 4Å MS (100 mg) were added and heated at 130 °C for 3.5 h. On completion of reaction, as confirmed by TLC, the reaction content was poured into ice cold water (40 mL) under stirring which resulted in generation of yellow precipitates. The yellow precipitates were filtered through Buchner funnel under suction and further purified by column chromatography on silica gel using EtOAc/hexane (10:90, v/v) as an eluent to obtain the pure product as a yellow solid, **4a** (0.295 g , 85% yield ; R_f = 0.62 (hexane/EtOAc, 70:30, v/v).

Procedure for the preparation of methyl 1-(benzo[d]thiazol-2-yl)-9-ethyl-9,9a-dihydro-4a*H*-pyrido[3,4-*b*]indole-3-carboxylate (**20n**). To a stirred the solution of methyl 9-ethyl-1-formyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (**20**; 0.200 g, 0.71 mmol) in DMSO (1.5 mL); 2-aminobenzenethiol (n; 0.097 g, 0.78 mmol), I_2 (0.036 g, 20 mol%, 0.14 mmol) and 4Å MS (100 mg) were added at room temperature for 8 h. The progress of reaction was monitored by TLC and after completion of reaction; the content was quenched with sodium thiosulfate (10% aqueous solution). Thereafter, reaction content was poured into ice cold water (40 mL) under stirring. The solid reaction mass was filtered through Buchner funnel to get the solid product which was further purified by column chromatography on silica gel using EtOAc/hexane (15:85, v/v) as an eluent to obtain the pure product as a yellow solid, **20n** (0.20 g, 72%; R_f = 0.68 (hexane/EtOAc, 70:30, v/v).

General procedure for the preparation of (*E*)-9-ethyl-*N*-((9-methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)methylene)-9*H*-carbazol-3-amine (**29**). To a stirred solution of 9-methyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde (**5;** 0.200 g, 0.95 mmol) in DMSO (1.5 mL); 3-amino-9-ethylcarbazole (**a;** 0.220 g, 1.05 mmol), S_8 (0.152 g, 4.76 mmol), I_2 (20 mol %, 0.048 g) and 4Å MS (100 mg), were added and heated the reaction mixture at 130 °C for 30 min. The progress of reaction was monitored by TLC and the reaction was quenched with sodium thiosulfate (10% aqueous solution**)** after 1.5 h to isolate the imine intermediate **29** midway. Thereafter, reaction content was poured into ice cold water (30 mL) under stirring which resulted formation of yellow precipitates. The yellow precipitate was filtered through Buckner funnel. Which was further purified by column chromatography on silica gel using (EtOAc/hexane 25:75, v/v) as an eluent to obtain the pure product as a yellow solid, **29** (0.305 g, 80% yield; R_f = 0.43 (hexane/EtOAc, 70 : 30, v/v) along with **5a** as (0.063 g, 15%; R_f = 0.78 (hexane/EtOAc, 70 : 30, v/v).

Procedure for the synthesis of (*E*)-9-ethyl-*N*-((9-methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)methylene)-9*H*-carbazol-3-amine (**29**). To stirred a solution of 1-(dimethoxymethyl)-9-methyl-9*H*-pyrido[3,4-*b*]indole (**28**; 0.200 g, 0.78 mmol) in anhydrous DMSO (1.5 mL); 3-amino-9ethylcarbazole (a; 0.180 g, 0.859 mmol), S_8 (0.125 g, 3.91 mmol), KI (0.026 g, 20 mol%) and 4Å MS (100 mg) were added and stirred the reaction mixture at 130 °C for 1.5 h. The progress of reaction was analysed by TLC and the reaction was quenched with ice cold water (20 mL) after 1.5 h in order to isolate the imine intermediate 29. The reaction mixture was poured into ice cold water (30 mL) under stirring which resulted in formation of yellow precipitates. The solid reaction mass was filtered through Buchner funnel and further purified by column chromatography on silica gel using EtOAc/hexane (25:75, v/v) as an eluent which afforded the imine intermediate in pure form as a yellow solid, **29** (0.225 g, 72%; R_f = 0.43 (hexane/EtOAc, 70 : 30, v/v) along with **5a** as (0.048 g, 14%; R_f = 0.78 (hexane/EtOAc, 70 : 30, v/v).

Procedure for the synthesis of 6-ethyl-2-(9-methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-6*H*-thiazolo[4,5-*c*]carbazole 5a from imine intermediate 29. To a stirred solution of (*E*)-9-ethyl-*N*-((9-methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)methylene)-9*H*-carbazol-3-amine (**29;** 0.200g, 0.50 mmol) in anhyrous DMSO (1.5 mL); S_8 (0.79 g, 2.49 mmol), I_2 (0.25 g, 20 mol%) and 4Å MS (100 mg) were added and stirred the reaction mixture for 2.5 h at 130 °C. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with sodium thiosulfate **(**10% aqueous solution**)**. Thereafter, the reaction content was poured into ice cold water (30 mL) under stirring which resulted in formation of yellow precipitates. The precipitates were filtered through Buckner funnel to get the solid product which was further purified by column chromatography on silica gel using EtOAc/hexane (10:90, v/v) as an eluent to obtain pure product as yellow solid, **5a** (0.212 g, 99% yield; R_f = 0.78 (hexane/EtOAc, 70:30, v/v). Similarly, reaction with KI (0.016 g, 20 mol%) as catalyst yielded the pure product as yellow solid **5a** in 91% yield (0.196 g).

Procedure for the preparation of 6-ethyl-2-(9-methyl-*9H*-pyrido[3,4-*b*]indol-1-yl)-6*H*-thiazolo[4,5-*c*]carbazole (5a) in presence of TEMPO. To a stirred the solution 1-(dimethoxymethyl)-9-methyl-9*H*-pyrido[3,4-*b*]indole (**28**; 0.20 g, 0.78 mmol) in anhyrous DMSO (1.5 mL); 3-amino-9-ethylcarbazole (**a** 0.180 g, 0.859 mmol), S_8 (0.125 g, 3.91 mmol), KI (0.026 g, 20 mol%), TEMPO (0.243 g, 1.56 mmol) and 4Å MS (100 mg) were added and stirred the reaction mixture at 130 °C for 5.5 h. On completion of reaction, as monitored by TLC, the reaction mixture was cooled to room temperature and the reaction content was poured into ice cold water (30 mL) under stirring. The reaction mass was filtered through Buckner funnel to get the solid product which was further purified by column chromatography on silica gel using EtOAc/hexane (10:90, v/v) as an eluent to obtain pure product as yellow solid, **5a** (0.33 g, 80% yield; R_f = 0.78 (hexane/EtOAc, 70:30, v/v).

9-Ethyl-9,9 a-dihydro-4a*H*-pyrido[3,4-*b*]indole-1-carbaldehyde (6). Yield: 84% (0.92 g from 1.0 g) as a light green solid; m.p. 98-100 °C; R_f = 0.71 (hexane/EtOAc, 90:10, v/v); IR (neat): ν_{max} (cm^{-1}) = 1689 (CHO); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.40 (t, *J* = 7.1 Hz, 3H, NCH_2CH_3), 4.89 (q, *J* = 7.1 Hz, 2H, NCH_2CH_3), 7.35 (t, *J* = 7.4 Hz, 1H, ArH), 7.54 (d, *J* = 8.3 Hz, 1H, ArH), 7.63–7.68 (m, 1H, ArH), 8.13–8.16 (m, 2H, ArH), 8.62–8.63 (m, 1H, ArH), 10.33 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 15.0, 41.9, 110.5, 118.8, 120.8, 121.0, 121.5, 129.5, 132.7, 135.0, 137.7, 138.4, 142.2, 194.2 ppm; HRMS (ESI) m/z: calcd. for $C_{14}H_{12}N_2O$ [M + H^+]: 225.1028, found: 225.1011.

9-Propyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde (7). Yield: 83% (1.0 g from 1.0 g) as a light yellow solid; m.p. 165-167 °C; R_f = 0.60 (hexane/EtOAc, 90:10, v/v); IR (neat): ν_{max} (cm^{-1}) = 1697 (CHO); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.92 (t, *J* = 7.4 Hz, 3H, $NCH_2CH_2CH_3$), 1.74–1.84 (m, 2H, $NCH_2CH_2CH_3$), 4.78–4.82 (m, 2H, $NCH_2CH_2CH_3$), 7.31–7.35 (m, 1H, ArH), 7.52 (d, *J* = 8.4 Hz, 1H, ArH), 7.62–7.66 (m, 1H, ArH), 8.11–8.15 (m, 2H, ArH), 8.62 (d, *J* = 4.8 Hz, 1H, ArH), 10.31 (s, 1H, CHO) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 11.2, 23.1, 48.3, 110.7, 118.7, 120.8, 121.4, 129.4, 132.5, 135.3, 137.7, 138.4, 142.6, 194.1 ppm; HRMS (ESI) m/z: calcd. for $C_{15}H_{14}N_2O$ [M + H^+]: 239.1184, found: 239.1154.

9-Butyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde (8). Yield: 85% (1.1 g from 1.0 g) as a light yellow solid; m.p. 62-65 °C; R_f = 0.60 (hexane/EtOAc, 90:10, v/v); IR (neat): ν_{max} (cm^{-1}) = 1703 (CHO); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.92 (t, *J* = 7.4 Hz, 3H, $NCH_2CH_2CH_2CH_3$), 1.31–1.40 (m, 2H, $NCH_2CH_2CH_2CH_3$), 1.71–1.75 (m, 2H, $NCH_2CH_2CH_2CH_3$), 4.85 (t, *J* = 7.62, 2H, $NCH_2CH_2CH_2CH_3$), 7.33–7,36 (m,1H), 7.63–7.67 (m, 1H, ArH), 8.13–8.16 (m, 2H, ArH), 8.63 (d, *J* = 4.9 Hz, 1H, ArH) 10.32 (s, 1H, CHO) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.0, 20.1, 31.9, 46.7, 110.7, 118.8, 120.9, 121.5, 129.4, 132.6, 135.3, 137.8, 138.4, 142.6, 194.1 ppm; HRMS (ESI) m/z: calcd. for $C_{16}H_{16}N_2O$ [M + H^+]: 253.1341, found: 253.1326.

9-Benzyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde (9). Yield: 87% (1.3 g from 1.0 g) as a light yellow solid; m.p. 120-122 °C; R_f = 0.60 (hexane/EtOAc, 90:10, v/v); IR (neat): ν_{max} (cm^{-1}) = 1698 (CHO); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.19 (s, 2H, CH_2Ar). 6.93–6.96 (m, 2H, ArH), 7.19 (d, *J* = 7.2 Hz, 3H, ArH), 7.38 (t, *J* = 7.5 Hz, 1H, ArH), 7.50 (d, *J* = 8.3 Hz, 1H, ArH), 7.60–7.63 (m, 1H, ArH), 8.21 (d, *J* = 7.7 Hz, 1H, ArH), 8.24 (d, *J* = 4.8 Hz, 1H, ArH), 8.68 (d, *J* = 4.9 Hz, 1H, ArH), 10.22 (s, 1H, CHO); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 50.2, 111.1, 118.9, 121.2, 121.5, 126.2, 127.1, 127.4, 127.6, 127.7, 128.7, 129.7, 130.2, 132.9, 135.8, 137.7, 138.1, 138.9, 143.0, 194.0 ppm; HRMS (ESI) m/z: calcd. for $C_{19}H_{14}N_2O$ [M + H^+]: 287.1184, found: 287.1152.

6-Ethyl-2-(9*H*-pyrido[3,4-*b*]indol-1-yl)-6*H*-thiazolo[4,5-*c*]carbazole (4a). Yield: 93% (0.19 g from 0.10 g) as a yellow solid; m.p. >250 °C; R_f = 0.62 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 3406 (NH), 1624 (C=N), 745 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.52 (t, *J* = 7.3 Hz, 3H; NCH_2CH_3), 4.51 (q, *J* = 7.2 Hz, 2H, NCH_2CH_3), 7.35 (t, *J* = 7.4 Hz, 1H, ArH), 7.39–7.43 (m, 1H), 7.53–7.59 (m, 2H, ArH), 7.62–7.65 (m, 2H, ArH) 7.73 (d, *J* = 8.1 Hz, 1H, ArH), 8.05 (d, *J* = 5.1 Hz, 1H, ArH), 8.20 (d, *J* = 7.8 Hz, 1H, ArH), 8.26 (d, *J* = 7.7 Hz, 1H, ArH), 8.31 (d, *J* = 8.8 Hz, 1H, ArH), 8.59 (d, *J* = 5.1 Hz, 1H, ArH), 10.79 (s, 1H, NH) ppm. The ^{13}C NMR spectrum could not be recorded due to solubility problem in $CDCl_3$ as well as DMSO-d_6; HRMS (ESI) m/z: calcd. for $C_{26}H_{18}N_4$ [M + H^+]: 419.1330, found: 419.1321.

Methyl 9-butyl-1-(5-ethyl-5*H*-thiazolo[4,5-*b*]carbazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (5a). Yield: 98% (0.40 g from 0.20 g) as a yellow solid; m.p. 196-198 °C; R_f = 0.78 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1621 (C=N), 718 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.50 (t, *J* = 6.9 Hz, 3H, NCH_2CH_3), 4.28 (s, 3H, NCH_3), 4.47 (q, *J* = 7.0 Hz, 2H, NCH_2CH_3), 7.34 (t, *J* = 7.3 Hz, 1H, ArH), 7.40 (t, *J* = 7.0 Hz, 1H, ArH), 7.54 (t, *J* = 8.1 Hz, 3H, ArH), 7.60 (d, *J* = 8.9 Hz, 1H, ArH), 7.64 (t, *J* = 7.7 Hz, 1H, ArH), 8.06 (d, *J* = 4.6 Hz, 1H, ArH), 8.17 (d, *J* = 7.7 Hz, 1H, ArH), 8.24 (t, *J* = 9.8 Hz, 2H, ArH), 8.61 (d, *J* = 4.7 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.2, 34.8, 38.1, 108.2, 109.0, 110.5, 115.6, 119.8, 120.3, 121.0, 121.1, 121.4, 121.5, 122.2, 125.6, 129.1, 129.3 132.3, 135.1, 136.4, 137.7, 138.3, 139.8, 143.9, 148.8, 165.6 ppm; HRMS (ESI) m/z: calcd. for $C_{27}H_{20}N_4S$ [M + H^+]: 433.1487, found: 433.1466.

6-Ethyl-2-(9-ethyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-6*H*-thiazolo[4,5-*c*] carbazole (6a). Yield: 92% (0.18 g from 0.10 g) as a yellow solid; m.p. 220-222 °C; R_f = 0.80 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) C=N (1618), C-S (732); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.33 (t, *J* = 7.1 Hz, 3H, $NCH_2CH_{3carbazole}$), 1.53 (t, *J* = 7.2 Hz, 3H, CH_2CH_3), 4.53 (q, *J* = 7.2 Hz, 2H, $NCH_2CH_{3carbazole}$), 5.15 (q, *J* = 7.1 Hz, 2H, NCH_2CH_3), 7.34–7.37 (m, 1H, ArH), 7.38–7.42 (m, 1H, ArH), 7.55–7.57 (m, 2H, ArH), 7.61–7.64 (m, 2H, ArH), 7.65–7.68 (m, 1H, ArH), 8.10 (d, *J* = 4.9 Hz, 1H, ArH), 8.19–8.24 (m, 2H, ArH), 8.28 (d, *J* = 7.6 Hz, 1H, ArH), 8.62 (d, *J* = 4.9 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.3, 14.9, 38.2, 41.3, 108.2, 109.1, 110.7, 115.6, 115.7, 119.9, 120.3, 121.1, 121.5, 121.6, 122.2, 125.7, 129.1, 129.4, 132.7, 133.9, 136.3, 137.8, 138.1, 139.8, 142.8, 148.9, 165.8 ppm; HRMS (ESI) m/z: calcd. for $C_{28}H_{22}N_4S$ [M + H^+]: 447.1643, found: 447.1658.

6-Ethyl-2-(9-propyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-6*H*-thiazolo[4,5-*c*] carbazole (7a). Yield: 93% (0.18 g from 0.10 g) as a yellow solid; m.p. 215-217 °C; R_f = 0.82 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) C=N (1623), C-S (731); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.76 (t, *J* = 7.4 Hz, 3H, $NCH_2CH_2CH_3$), 1.53 (t, *J* = 7.3 Hz, 3H, NCH_2CH_3), 1.71–1.81 (m, 2H, $NCH_2CH_2CH_3$), 4.52 (q, *J* = 7.2 Hz, 2H, NCH_2CH_3), 5.09 (t, *J* = 7.7 Hz, 2H, $NCH_2CH_2CH_3$), 7.33–7.36 (m, 1H, ArH), 7.38–7.42 (m, 1H, ArH), 7.54–7.57 (m, 2H, ArH), 7.59–7.68 (m, 3H, ArH), 8.11 (d, *J* = 4.9 Hz, 1H, ArH), 8.20 (d, *J* = 7.8 Hz, 1H, ArH), 8.23 (d, *J* = 8.6 Hz, 1H, ArH), 8.28 (d, *J* = 7.5 Hz, 1H, ArH), 8.62 (d, *J* = 4.9 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 11.3, 14.3, 23.1, 38.2, 47.8, 108.2, 109.0, 110.8, 115.7, 119.8, 120.2, 121.0, 121.2, 121.4, 121.6, 122.2, 125.6, 128.9, 129.4, 131.0, 132.4, 134.0, 136.3, 137.7, 138.1, 139.8, 143.1, 149.0, 166.1 ppm; HRMS (ESI) m/z: calcd. for $C_{29}H_{24}N_4S$ [M + H^+]: 461.1800, found: 461.1790.

2-(9-Butyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-6-ethyl-6*H*-thiazolo[4,5-*c*]carbazole (8a). Yield: 85% (0.16 g from 0.10) g as a yellow solid; m.p. 178-180 °C; R_f = 0.85 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) 1619 (C=N), 656 (C-S); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.76 (t, *J* = 7.4 Hz, 3H, $NCH_2CH_2CH_2CH_3$), 1.15–1.22 (m, 2H, $NCH_2CH_2CH_2CH_3$), 1.51 (t, *J* = 7.2 Hz, 3H, NCH_2CH_3), 1.67–1.72 (m, 2H, $NCH_2CH_2CH_2CH_3$), 4.49 (q, *J* = 7.2 Hz, 2H, NCH_2CH_3), 5.12 (t, *J* = 7.7 2H, $NCH_2CH_2CH_2CH_3$), 7.34 (t, *J* = 7.3 Hz, 1H, ArH), 7.39–7.42 (m, 1H, ArH), 7.52–7.56 (m, 2H, ArH), 7.58–7.61 (m, 2H, ArH), 7.65 (t, *J* = 7.5 Hz, 1H; ArH), 8.09 (d, *J* = 4.9 Hz, 1H, ArH), 8.20 (t, *J* = 9.1 Hz, 2H, ArH), 8.29 (d, *J* = 7.8 Hz, 1H, ArH), 8.62 (d, *J* = 5.0 Hz, 1H, ArH) ppm; ^{13}C NMR (125 MHz,$CDCl_3$) δ = 14.0, 14.3, 20.2, 31.9, 38.2, 46.1, 108.2, 109.1, 110.8, 115.7, 119.9, 120.2, 121.0, 121.3, 121.5, 122.2, 125.6, 129.0, 129.4, 132.5, 134.0, 136.3, 137.7, 138.1, 139.8, 143.0, 149.0, 166.1 ppm; HRMS (ESI) m/z: calcd. for $C_{30}H_{26}N_4S$ [M + H^+]: 475.1956, found: 4751955.

2-(9-Benzyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-5-ethyl-5*H*-thiazolo[4,5-*b*]carbazole (9a). Yield: 84% (0.22 g from 0.15) as a yellow solid; m.p. 188-190 °C; R_f = 0.79 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) 1621 (C=N), 732 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.51 (t, *J* = 7.2 Hz, 3H, NCH_2CH_3). 4.49 (q, *J* = 7.2 Hz, 2H, NCH_2CH_3), 6.40 (s, 2H, CH_2Ar), 6.84–6.86 (m, 2H, ArH), 7.04–7.11 (m, 3H, ArH), 7.35–7.40 (m, 2H, ArH), 7.51–7.57 (m, 4H, ArH), 7.59–7.63 (m, 1H, ArH), 7.90 (d, *J* = 8.9 Hz, 1H, ArH), 8.12 (d, *J* = 5.0 Hz, 1H, ArH), 8.22 (dd, J_1 = 7.7 J_2 = 3.8 Hz, 2H, ArH), 8.63 (d, *J* = 4.9 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.2, 38.1, 50.1, 108.1, 109.0, 111.4, 115.5, 115.7, 119.8, 120.7, 121.0, 121.5, 121.5, 122.2, 125.6, 126.3, 126.9, 127.0, 128.4, 128.9, 129.2, 129.4, 132.8, 134.6, 136.7, 137.7, 138.4, 138.6, 139.8, 143.7, 148.7, 165.7 ppm; HRMS (ESI) m/z: calcd. for $C_{33}H_{24}N_4S$ [M + H^+]: 509.1800, found: 509.1790.

Methyl 1-(6-ethyl-6*H*-thiazolo[4,5-*c*]carbazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (11a). Yield: 87% (0.16 g from 0.10 g) as a yellow solid; m.p. >250 °C; R_f = 0.60 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1717 (CO_2CH_3), 3375 (NH), 1610 (C=N), 736 (C-S); δ = ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.51 (t, *J* = 7.2 Hz, 3H, NCH_2CH_3), 4.15 (s, 3H, CO_2CH_3), 4.47 (q, *J* = 7.2 Hz, 2H, NCH_2CH_3), 7.38–7.44 (m, 2H, ArH), 7.52–7.57 (m, 2H, ArH), 7.60 (d, *J* = 9.0 Hz, 1H, ArH), 7.66 (t, *J* = 7.6 Hz, 1H, ArH), 7.74 (d, *J* = 8.2 Hz, 1H, ArH), 8.23 (d, *J* = 7.9 Hz, 1H, ArH), 8.28 (t, *J* = 8.8 Hz, 2H, ArH), 8.92 (s, 1H, ArH), 11.01 (s, 1H, ArH) ppm; ^{13}C NMR spectra could not be recorded due to solubility problem in $CDCl_3$ & DMSO-d_6; HRMS (ESI) m/z: calcd. for $C_{28}H_{20}N_4O_2S$ [M + Na^+]: 499.1205, found: 499.1202.

Methyl 1-(5-ethyl-5*H*-thiazolo[4,5-*b*]carbazol-2-yl)-9-methyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (19a). Yield: 80% (0.22 g from 0.15 g) as a yellow solid; m.p. 199-200 °C; R_f = 0.64 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1708 (CO_2CH_3), 1620 (C=N), 739 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.50 (t, *J* = 7.2 Hz, 3H, NCH_2CH_3) 4.13 (s, 3H, CO_2CH_3), 4.27 (s, 3H, NCH_3), 4.46 (q, *J* = 7.0 Hz, 2H, NCH_2CH_3), 7.40 (t, *J* = 7.1 Hz, 2H, ArH), 7.51–7.54 (m, 2H, ArH). 7.56–7.58 (m, 2H, ArH), 7.67 (t, *J* = 7.5 Hz, 1H, ArH), 8.21 (d, *J* = 8.3 Hz, 2H, ArH), 8.26 (d, *J* = 7.7 Hz, 1H, ArH), 8.90 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.3, 34.9, 38.2, 53.0, 108.3, 109.1, 110.7, 118.1, 119.9, 121.1, 121.3, 121.3, 121.6, 122.1, 125.7, 128.9, 129.5, 129.7, 131.0, 132.3,

136.0, 136.2, 136.7, 137.8, 139.8, 144.0, 148.7, 164.5, 166.3 ppm; HRMS (ESI) m/z: calcd. for $C_{29}H_{22}N_4O_2S$ [M + H$^+$]: 491.1542, found: 491.15.

Methyl 9-ethyl-1-(5-ethyl-5*H*-thiazolo[4,5-*b*]carbazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (20a). Yield: 83% (0.29 g from 0.20 g) as a yellow solid; m.p. 195-196 °C; R_f = 0.68 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1707 (CO_2CH_3), 1622 (C=N), 723 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.35 (t, J = 7.1 Hz, 3H, $NCH_2CH_{3carbazole}$), 1.54 (t, J = 7.3 Hz, 3H, CH_2CH_3), 4.14 (s, 3H, CO_2CH_3), 4.53 (q, J = 7.2 Hz, 2H, $NCH_2CH_{3carbazole}$), 5.15 (q, J = 7.1 Hz, 2H, NCH_2CH_3), 7.40–7.44 (m, 2H, ArH), 7.56–7.58 (m, 2H, ArH), 7.62–7.66 (m, 2H, ArH), 7.68–7.72 (m, 1H, ArH), 8.22 (d, J = 8.8 Hz, 1H, ArH), 8.27 (d, J = 7.8 Hz, 1H, ArH), 8.30–8.32 (m, 1H, ArH), 8.98 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.2, 15.0, 38.1, 41.5, 53.0, 108.2, 109.0, 110.9, 115.5, 118.1, 119.8, 121.0, 121.2, 121.7, 122.1, 125.6, 128.9, 129.4, 129.8 131.0, 132.6, 135.0, 135.9, 136.5, 137.7, 139.7, 142.8, 148.7, 164.8, 166.2 ppm; HRMS (ESI) m/z: calcd. for $C_{30}H_{24}N_4O_2S$ [M + H$^+$]: 505.1698 found: 505.1664.

Methyl 1-(5-ethyl-5*H*-thiazolo[4,5-*b*]carbazol-2-yl)-9-propyl-9*H*-pyrido [3,4-*b*]indole-3-carboxylate (21a). Yield: 75% (0.26 g from 0.20 g) as a yellow solid; m.p. 194-196 °C; R_f = 0.72 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1701 (CO_2CH_3), 1623 (C=N), 734 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.75 (t, J = 7.4 Hz, 3H, $NCH_2CH_2CH_3$), 1.52 (t, J = 7.2 Hz, 3H, NCH_2CH_3), 1.76 (m, 2H, $NCH_2CH_2CH_3$), 4.15 (s, 3H, CO_2CH_3), 4.48 (q, J = 7.2, 2H, NCH_2CH_3), 5.06 (t, J = 7.7, 2H, $NCH_2CH_2CH_3$), 7.39 (d, J = 7.4 Hz, 1H, ArH), 7.41–7.43 (m, 1H, ArH), 7.54 (t, J = 8.5 Hz, 2H, ArH), 7.58–7.61 (m, 2H, ArH), 7.67 (t, J = 7.6 Hz, 1H, ArH), 8.20 (d, J = 8.7 Hz, 1H, ArH), 8.24 (d, J = 7.8 Hz, 1H, ArH), 8.30 (d, J = 7.7 Hz, 1H, ArH), 8.96 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 11.3, 14.3, 23.2, 38.1, 47.9, 53.0, 108.3, 109.1, 110.1, 115.6, 118.1, 119.9, 121.0, 121.2, 121.5, 121.7, 122.1, 125.7, 129.4, 129.9, 132.5, 135.2, 136.9, 136.5, 137.8, 139.8, 143.2, 148.8, 165.0, 166.3 ppm; HRMS (ESI) m/z: calcd. for $C_{31}H_{26}N_4O_2S$ [M + H$^+$]: 519.1855, found: 519.1868.

Methyl 9-butyl-1-(5-ethyl-5*H*-thiazolo [4,5-*b*]carbazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (22a). Yield: 70% (0.24 g from 0.20 g) as a yellow solid; m.p. 174-176 °C; R_f = 0.76 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1702 (CO_2CH_3), 1615 (C=N), 743 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.73 (t, J = 7.1 Hz, 3H, $NCH_2CH_2CH_2CH_3$), 1.12–1.22 (m, 2H, $NCH_2CH_2CH_2CH_3$), 1.53 (t, J = 6.9 Hz, 3H, NCH_2CH_3), 1.60–1.70 (m, 2H, $NCH_2CH_2CH_2CH_3$), 4.14 (s, 3H, CO_2CH_3), 4.51 (q, J = 6.7 Hz, 2H, NCH_2CH_3), 5.12 (t, J = 7.2 Hz, 2H, $NCH_2CH_2CH_2CH_3$), 7.41–7.57 (m, 4H, ArH), 7.62 (d, J = 8.5 Hz, 2H, ArH), 7.69 (t, J = 7.4 Hz, 1H, ArH), 8.20 (d, J = 8.7 Hz, 1H, ArH), 8.26 (d, J = 7.6 Hz, 1H, ArH), 8.31 (d, J = 7.6 Hz, 1H, ArH), 8.98 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 13.9, 14.3, 20.2, 31.9, 38.1, 46.3, 53.0, 108.3, 109.0, 111.1, 115.6, 118.1, 119.9, 121.0, 121.2, 121.6, 121.7, 122.1, 122.7, 129.4, 129.8, 132.6, 135.2, 136.0, 136.5, 137.8, 139.8, 143.2, 148.7, 165.1, 166.3 ppm; HRMS (ESI) m/z: calcd. for $C_{32}H_{28}N_4O_2S$ [M + Na$^+$]: 555.1831, found: 555.1811.

Methyl 9-benzyl-1-(6-ethyl-6*H*-thiazolo [4,5-*c*]carbazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (23a). Yield: 88% (0.145 g from 0.10) as a yellow solid; m.p. 180-182 °C; R_f = 0.78 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1702 (CO_2CH_3), 1626 (C=N), 731 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.52 (t, J = 7.2 Hz, 3H, NCH_2CH_3), 4.13 (s, 3H, CO_2CH_3), 4.50 (q, J = 7.2 Hz, 2H, NCH_2CH_3), 6.42 (s, 2H, CH_2Ar), 6.76 (d, J = 7.1 Hz, 2H, ArH), 6.99–7.03 (m, 2H, ArH), 7.04–7.08 (m, 1H, ArH), 7.38–7.42 (m, 1H, ArH), 7.45 (d, J = 7.6 Hz, 1H, ArH), 7.55–7.56 (m, 2H, ArH), 7.58–7.61 (m, 2H, ArH), 7.64–7.68 (m, 1H, ArH), 7.96 (d, J = 8.9 Hz, 1H, ArH), 8.24 (d, J = 7.7 Hz, 1H, ArH), 8.30 (d, J = 7.8 Hz, 1H, ArH), 9.00 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.3, 38.2, 50.1, 53.1, 108.3, 109.0, 111.6, 115.5, 118.1, 119.8, 121.0, 121.6, 121.8, 122.1, 125.6, 126.2, 127.2, 128.5, 129.7, 129.8, 133.0, 135.7, 136.5, 137.1, 137.7, 137.8, 139.8, 143.9, 148.6, 164.7, 166.2 ppm; HRMS (ESI) m/z: calcd. for $C_{35}H_{26}N_4O_2S$ [M + H$^+$]: 567.185, found: 567.18.

Methyl 1-(6-ethyl-6*H*-thiazolo[4,5-*c*]carbazol-2-yl)-9-(prop-2-yn-1-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (24a). Yield: 31% (0.11 g from 0.20) as a light Orange solid; m.p. 200-202 °C; R_f = 0.61 (hexane/EtOAc, 70:30, v/v) IR (neat): ν_{max} (cm^{-1}) = 1705 (CO_2CH_3), 1628 (C=N), 738 (C-S); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.54 (t, J = 7.2 Hz, 3H, NCH_2CH_3), 2.13 (t, J = 2.2 Hz, 1H, C≡CH), 4.15 (s, 3H, CO_2CH_3), 4.52 (q, J = 7.2 Hz, 2H, NCH_2CH_3), 6.17 (d, J = 2.1 Hz, 2H, NCH_2), 7.52–7.54 (m, 1H, ArH), 7.56–7.57 (m, 2H, ArH), 7.63 (d, J = 8.8 Hz, 1H, ArH), 7.70–7.77 (m, 3H, ArH), 8.25–8.27 (m, 2H, ArH), 8.31 (d, J = 7.5 Hz, 1H, ArH), 8.95 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz,$CDCl_3$) δ = 14.3, 37.0, 38.2, 53.1, 72.9, 78.8, 108.4, 109.1, 110.5, 111.4, 115.6, 118.1, 119.9, 121.2, 121.7, 121.8, 122.0, 122.2, 125.7, 129.8, 133.4, 135.0, 136.3, 137.5, 137.9, 138.9, 139.8, 143.1, 148.8, 150.1, 165.5, 166.1, ppm; HRMS (ESI) m/z: calcd. for $C_{31}H_{22}N_4O_2S$ [M + H$^+$]: 515.1542, found: 515.1511.

2-(9-Methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)naphtho[2,1-*d*]thiazole (5b). Yield: 77% (0.20 g from 0.15) as a yellow solid; m.p. 196-198 °C; R_f = 0.74 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1623 (C=N), 727 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.27 (s, 3H, CO_2CH_3). 7.34–7.38 (m, 1H, ArH), 7.55–7.58 (m, 1H, ArH), 7.59–7.61 (m, 1H, ArH), 7.63–7.65 (m, 1H, ArH), 7.66–7.69 (m, 1H, ArH), 7.93 (d, J = 8.8 Hz, 1H, ArH), 7.99–8.01 (m, 1H, ArH), 8.10 (d, J = 5.0 Hz, 1H, ArH), 8.15–8.16 (m, 1H, ArH), 8.17–8.20 (m, 2H, ArH), 8.60 (d, J = 4.9 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 34.9, 110.5, 116.0, 120.5, 121.1, 121.5, 122.0, 125.7, 126.4, 127.3, 127.4, 128.4, 129.1, 129.2, 131.3, 132.5, 133.7, 135.2, 135.9, 138.4, 143.9, 152.1, 168.6 ppm; HRMS (ESI) m/z: calcd. for $C_{23}H_{15}N_3S$ [M + H$^+$]: 366.1065, found: 366.1071.

2-(9-Ethyl-9*H*-pyrido[3,4-*b*]indol-1-yl)naphtho[2,1-*d*]thiazole (6b).
Yield: 88% (0.15 g from 0.10) as a brown solid; m.p. 138-142 °C; R_f = 0.73 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1664 (C=N), 739 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.33 (t, J = 7.0 Hz, 3H, NCH_2CH_3), 5.11 (q, J = 7.0 Hz, 2H, NCH_2CH_3), 7.33–7.37 (m, 1H, ArH), 7.57–7.62 (m, 2H, ArH), 7.63–7.69 (m, 2H, ArH), 7.92 (d, J = 8.8 Hz, 1H, ArH), 8.01 (d, J = 7.8 Hz, 1H, ArH), 8.10–8.15 (m, 2H, ArH), 8.19 (t, J = 8.1 Hz, 2H, ArH), 8.59 (d, J = 5.1 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.9, 41.3, 110.7, 116.0, 120.4, 121.4, 121.6, 122.0, 125.7, 126.4, 127.2, 127.3, 128.3, 129.1, 131.3, 132.8, 133.8, 133.9, 135.9, 138.2, 142.8, 152.2, 169.0 ppm; HRMS (ESI) m/z: calcd. for $C_{24}H_{17}N_3S$ [M + H$^+$] 380.1221, found: 380.1206.

2-(9-Propyl-9*H*-pyrido[3,4-*b*]indol-1-yl)naphtho[2,1-*d*]thiazole (7b). Yield: 78% (0.129 g from 0.10 g) as a yellow solid; m.p. 181-183 °C; R_f = 0.78 (hexane/EtOAc, 70:30, v/v) IR (neat): ν_{max} (cm^{-1}) = 1620 (C=N), 739 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.76 (t, J = 7.4 Hz, 3H, $NCH_2CH_2CH_3$), 1.69–1.80 (m, 2H, $NCH_2CH_2CH_3$), 5.05 (t, J = 7.7 2H, $NCH_2CH_2CH_3$), 7.35 (t, J = 7.4 Hz, 1H, ArH), 7.57–7.61 (m, 2H, ArH), 7.63–7.68 (m, 2H, ArH), 7.92 (d, J = 8.8 Hz, 1H; ArH), 8.01 (d, J = 8.0 Hz, 1H, ArH), 8.12–8.21 (m, 4H, ArH), 8.59 (d, J = 4.9 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 11.3, 23.0, 47.8, 110.8, 116.0, 120.3, 121.1, 121.5, 121.9, 125.7, 126.4, 127.2, 127.4, 128.3, 129.1, 131.3, 132.6, 133.8, 134.0, 135.8, 138.1 143.1, 152.2, 169.1 ppm; HRMS (ESI) m/z: calcd. for $C_{25}H_{19}N_3S$ [M + H$^+$] 394.1378, found: 394.1384.

2-(9-Butyl-9*H*-pyrido[3,4-*b*]indol-1-yl)naphtho[2,1-*d*]thiazole (8b). Yield: 79% (0.191 g from 0.15) as a yellow solid; m.p. 158-160 °C; R_f = 0.81 (hexane/EtOAc, 70:30, v/v) IR (neat): ν_{max} (cm^{-1}) 1580 (C=N), 672 (C-S); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.76 (t, J = 7.4 Hz, 3H, $NCH_2CH_2CH_2CH_3$), 1.13–1.22 (m, 2H, $NCH_2CH_2CH_2CH_3$), 1.64–1.71 (m, 2H, $NCH_2CH_2CH_2CH_3$), 5.08 (t, J = 7.7 Hz, 2H, $NCH_2CH_2CH_2CH_3$), 7.34 (t, J = 7.4 Hz, 1H, ArH), 7.57–7.60 (m, 2H, ArH), 7.63–7.67 (m, 2H, ArH), 7.91 (d, J = 8.8 Hz, 1H, ArH), 8.00 (d, J = 8.0 Hz, 1H, ArH), 8.10 (d, J = 4.9 Hz, 1H, ArH), 8.12 (d, J = 8.7 Hz, 1H, ArH), 8.18 (dd, J_1 = 7.8, J_2 = 2.6 Hz, 2H, ArH), 8.59 (d, J = 4.9 Hz, 1H, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 14.0, 20.1, 31.8, 46.1, 110.8, 116.0 120.3, 121.2, 121.5, 121.9, 125.7, 126.4, 127.2, 127.4, 128.3, 129.1, 131.3, 132.7, 133.8, 134.0, 135.8, 138.1, 143.0, 152.2, 169.1 ppm; HRMS (ESI) m/z: calcd. for $C_{26}H_{21}N_3S$ [M + H$^+$]: 408.1534, found: 408.1512.

2-(9-Benzyl-9*H*-pyrido[3,4-*b*]indol-1-yl)naphtho[2,3-*d*]thiazole (9b). Yield: 88% (0.20 g from 0.15) as a yellow solid; m.p. 205-210 °C; R_f = 0.74 (hexane/EtOAc, 70:30, v/v) IR (neat): ν_{max} (cm^{-1}) 1620 (C=N), 729 (C-S); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.34 (s, 2H, CH_2Ar). 6.80 (d, *J* = 7.1 Hz, 2H, ArH), 7.03–7.11 (m, 3H, ArH), 7.37 (t, *J* = 7.3 Hz, 1H, ArH), 7.53–7.58 (m, 2H, ArH), 7.60–7.63 (m, 2H, ArH), 7.82–7.86 (m, 2H, ArH), 7.97 (d, *J* = 7.9 Hz, 1H, ArH), 8.09 (d, *J* = 7.9 Hz, 1H, ArH), 8.13 (d, *J* = 5.0 Hz, 1H, ArH), 8.22 (d, *J* = 7.8 Hz, 1H, ArH), 8.60 (d, *J* = 4.9 Hz, 1H, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 50.1, 111.3, 116.0, 120.8, 121.5, 121.6, 121.9, 125.7, 126.2, 126.3, 127.0, 127.2, 127.3, 128.3, 128.5, 129.1, 129.4, 131.3, 133.0, 133.8, 134.6, 136.3, 138.2, 138.7, 143.7, 152.0, 168.6 ppm; HRMS (ESI) m/z: calcd. for $C_{29}H_{19}N_3S$ [M + H^+]: 442.1378, found: 442.1377.

Methyl 9-methyl-1-(naphtho[2,3-*d*]thiazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (19b). Yield: 70% (0.17 g from 0.15 g) as a brown solid; m.p. 210-212 °C; R_f = 0.64 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1711 (CO_2CH_3) 1618 (C=N), 739 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.11 (s, 3H, CO_2CH_3), 4.30 (s, 3H, NCH_3), 7.43 (t, *J* = 7.6 Hz, 1H, ArH), 7.58–7.63 (m, 2H, ArH), 7.64–7.68 (m, 1H, ArH), 7.69–7.73 (m, 1H, ArH), 7.93 (d, *J* = 8.8 Hz, 1H, ArH), 8.01 (d, *J* = 7.8 Hz, 1H, ArH), 8.15 (d, *J* = 8.9 Hz, 1H, ArH), 8.20 (d, *J* = 8.0 Hz, 1H, ArH), 8.26 (d, *J* = 7.9 Hz, 1H, ArH), 8.97 (s, 1H, ArH), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 35.0, 53.0, 110.8, 118.4, 121.4, 121.8, 122.0, 125.8, 126.6, 127.3, 127.6, 128.2, 129.1, 129.7, 131.4, 132.6, 134.2, 135.6, 136.3, 136.8, 144.0, 152.0, 166.2, 167.5 ppm; HRMS (ESI) m/z: calcd. for $C_{25}H_{17}N_3O_2S$ [M + H^+]: 424.1120, found: 424.1090.

Methyl 9-ethyl-1-(naphtho[2,3-*d*]thiazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (20b). Yield: 76% (0.12 g from 0.10 g) as a yellow solid; m.p. 194-195 °C; R_f = 0.70 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1719 (CO_2CH_3); 1613 (C=N), 737 (C-S); 1H NMR (400 MHz, $CDCl_3$) δ = 1.35 (t, *J* = 7.1 Hz, 3H, NCH_2CH_3), 4.12 (s, 3H, CO_2CH_3), 5.12 (q, *J* = 7.1 Hz, 2H, NCH_2CH_3), 7.40–7.44 (m, 1H, ArH), 7.58–7.64 (m, 2H, ArH), 7.65–7.66 (m, 1H, ArH), 7.67–7.72 (m, 1H, ArH), 7.92 (d, *J* = 8.8 Hz, 1H, ArH), 8.01 (d, *J* = 7.7 Hz, 1H, ArH), 8.13 (d, *J* = 8.8 Hz, 1H, ArH), 8.21 (d, *J* = 8.0 Hz, 1H, ArH), 8.26 (d, *J* = 7.8 Hz, 1H, ArH), 8.98 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 15.0, 41.5, 53.0, 111.1, 118.5, 121.4, 121.8, 121.9, 122.0, 125.9, 126.6, 127.4, 127.6, 128.4, 129.2, 129.7, 131.5, 133.0, 134.4, 135.2, 135.5, 136.7, 143.0, 152.1, 166.3, 168.0 ppm; HRMS (ESI) m/z: calcd. for $C_{26}H_{19}N_3O_2S$ [M + H^+]: 438.1276, found: 438.1287.

Methyl 1-(naphtho[2,1-*d*]thiazol-2-yl)-9-propyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (21b). Yield: 95% (0.14 g from 0.10) as a yellow solid; m.p. 198-200 °C; R_f = 0.73 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1737 (CO_2CH_3), 1618 (C=N), 735 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.76 (t, *J* = 7.4 Hz, 3H,$NCH_2CH_2CH_3$), 1.71–1.81 (m, 2H, $NCH_2CH_2CH_3$), 4.12 (s, 3H, CO_2CH_3), 5.07 (t, *J* = 7.7 Hz 2H, $NCH_2CH_2CH_3$), 7.42 (t, *J* = 7.2 Hz, 1H, ArH), 7.59–7.66 (m, 1H, ArH), 7.68–7.72 (m, 3H, ArH), 7.93 (d, *J* = 8.8 Hz, 1H, ArH), 8.01 (d, *J* = 7.7 Hz, 1H, ArH), 8.14 (d, *J* = 8.7 Hz, 1H, ArH), 8.21 (d, *J* = 8.0 Hz, 1H, ArH), 8.27 (d, *J* = 7.8 Hz, 1H, ArH), 8.99 (s, 1H, ArH), ^{13}C NMR (100 MHz, $CDCl_3$) δ = 11.2, 23.1, 48.0, 53.0, 110.1, 118.4, 121.3, 121.3, 121.5, 121.7, 121.9, 125.8, 126.5, 127.3, 128.3, 129.1, 129.5, 131.4, 132.8, 134.4, 135.2, 135.4, 136.5, 143.2, 152.1, 166.2, 168.1 ppm; HRMS (ESI) m/z: calcd. for $C_{27}H_{21}N_3O_2S$ [M + H^+]: 452.1433, found: 452.1411.

Methyl 9-butyl-1-(naphtho[2,1-*d*] thiazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (22b). Yield: 89% (0.13 g from 0.10) as a yellow solid; m.p. 194-196 °C; R_f = 0.76 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1709 (CO_2CH_3), 1621 (C=N), 739 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.74 (t, *J* = 7.4 Hz, 3H, $NCH_2CH_2CH_2CH_3$), 1.11–1.20 (m, 2H, $NCH_2CH_2CH_2CH_3$), 1.64–1.72 (m, 2H, $NCH_2CH_2CH_2CH_3$), 4.12 (s, 3H, CO_2CH_3), 5.11 (t, *J* = 7.7 2H, $NCH_2CH_2CH_2CH_3$), 7.42 (t, *J* = 7.3 Hz, 1H, ArH), 7.59–7.66 (m, 3H, ArH), 7.68–7.72 (m, 1H, ArH), 7.93 (d, *J* = 8.8 Hz, 1H, ArH), 8.01 (d, *J* = 7.9 Hz, 1H, ArH), 8.12 (d, *J* = 8.9 Hz, 1H, ArH), 8.22 (d, *J* = 8.0 Hz, 1H, ArH), 8.27 (d, *J* = 7.8 Hz, 1H, ArH), 8.99 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.0, 20.2, 31.9, 46.4, 53.1, 111.2, 118.5, 121.4, 121.6, 121.8, 121.9, 125.9, 126.6, 127.4, 127.6, 128.4, 129.2, 129.6, 131.5, 132.9, 134.4, 135.3, 135.5, 136.6, 143.3, 152.1, 166.2, 168.1 ppm; HRMS (ESI) m/z: calcd. for $C_{28}H_{23}N_3O_2S$ [M + H^+]: 466.1589, found: 466.1541.

Methyl 9-benzyl-1-(naphtho[2,1-*d*] thiazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (23b). Yield: 75% (0.11 g from 0.10) as a light yellow solid; m.p. 190-192 °C; R_f = 0.79 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1708 (CO_2CH_3), 1622 (C=N), 732 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.11 (s, 3H, CO_2CH_3), 6.38 (s, 2H, CH_2Ar), 6.72 (d, *J* = 7.2 Hz, 2H, ArH), 6.98–7.02 (m, 2H, ArH), 7.05–7.09 (m,1H, ArH), 7.42–7.46 (m, 1H, ArH), 7.56–7.58 (m, 1H, ArH), 7.60–7.63 (m, 2H, ArH), 7.64–7.68 (m, 1H, ArH), 7.85–7.90 (m, 2H, ArH), 7.97–7.99 (m, 1H, ArH), 8.12 (d, *J* = 7.6 Hz, 1H, ArH), 8.30 (d, *J* = 7.8 Hz, 1H, ArH), 9.01 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz,$CDCl_3$) δ = 50.0, 53.0, 111.5, 118.4, 121.7, 121.8, 125.7, 126.1, 126.5, 127.2, 127.5, 128.2, 128.5, 129.0, 129.8, 131.3, 133.2, 134.4, 135.7, 136.0, 137.1, 137.5, 143.9, 151.8, 166.1, 167.6 ppm; HRMS (ESI) m/z: calcd. for $C_{31}H_{21}N_3O_2S$ [M + H^+]: 500.1433, found: 500.1385.

5,6-Dimethoxy-2-(9*H*-pyrido[3,4-*b*] indol-1-yl)benzo[*d*]thiazole (4d). Yield: 86% (0.16 g from 0.10 g) as a brown solid; m.p. 205–208 °C; R_f = 0.53 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 3372 (NH); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.01 (s, 3H, OCH_3). 4.06 (s, 3H, OCH_3), 7.33–7.37 (m, 1H, ArH), 7.38 (s, 1H, ArH), 7.62 (t, *J* = 7.5 Hz, 1H, ArH), 7.65 (s, 1H, ArH), 7.68 (d, *J* = 8.2 Hz, 1H, ArH), 8.02 (d, *J* = 5.1 Hz, 1H, ArH), 8.18 (d, *J* = 7.8 Hz, 1H, ArH), 8.52 (d, *J* = 5.0 Hz, 1H, ArH), 10.68 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 56.3, 56.5, 102.8, 104.7, 112.2, 116.1, 120.5, 121.4, 122.1, 127.5, 129.0, 130.5, 133.3, 138.9, 141.0, 148.8, 149.1, 149.6 ppm; HRMS (ESI) m/z: calcd. for $C_{20}H_{15}N_3O_2S$ [M + H^+]: 362.0963, found: 362.0955.

2-(9-Methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-6,7-dihydro-[1,4]dioxino[2',3':4,5] benzo[1,2-*d*]thiazole. **(5g)** Yield: 57% (0.10 g from 0.10 g) as a yellow solid; m.p. 215-220 °C; R_f = 0.67 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1624 (C=N), 741 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.15 (s, 3H, NCH_3), 4.35 (s, 4H, $(OCH_2)_2Ar$), 7.33 (t, *J* = 7.4 Hz, 1H, ArH), 7.43 (s, 1H, ArH), 7.53 (d, *J* = 8.3 Hz, 1H, ArH), 7.62–7.66 (m, 2H, ArH), 8.04 (d, *J* = 4.8 Hz, 1H, ArH), 8.15 (d, *J* = 7.7 Hz, 1H, ArH), 8.53 (d, *J* = 4.9 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 34.7, 64.4, 64.6, 108.7, 110.5, 110.7, 115.8, 120.4, 121.1, 121.5, 129.1, 129.4, 132.3, 135.2, 136.1, 138.3, 143.6, 144.0, 149.1, 168.1 ppm; HRMS (ESI*)* m/z: calcd. for $C_{21}H_{15}N_3O_2S$ [M + H^+]: 374.0963, found: 374.0953.

Methyl 1-(5,6-dimethoxybenzo[*d*] thiazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (11d). Yield: 87% (0.14 g from 0.10 g) as a yellow solid; m.p. 238-240 °C; R_f = 0.59 (hexane/EtOAc, 90:10, v/v); IR (neat): ν_{max} (cm^{-1}) = 1710 (CO_2CH_3), 3399 (NH), 1626 (C=N), 742 (C-S); δ = ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.00 (s, 3H, OCH_3), 4.05 (s, 3H, OCH_3), 4.10 (s, 3H, CO_2CH_3), 7.34 (s, 1H, ArH), 7.37–7.41 (m, 1H, ArH), 7.62 (d, *J* = 4.5 Hz, 1H, ArH), 7.65–7.67 (m, 1H, ArH), 7.69–7.71 (m, 1H, ArH), 8.21 (d, *J* = 7.8 Hz, 1H, ArH), 8.89 (s, 1H, ArH), 10.87 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 53.0, 56.3, 56.5, 102.6, 104.6, 112.5, 118.8, 121.4, 122.2, 127.8, 128.9, 129.5, 130.6, 131.0, 134.5, 137.5, 141.2, 148.5, 149.3, 149.7, 166.4, 167.1 ppm; HRMS (ESI) m/z: calcd. for $C_{22}H_{17}N_3O_4S$ [M + H^+]: 420.1018, found: 420.1026.

Methyl 1-(6-methoxybenzo[*d*]thiazol-2-yl)-9-methyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate. **(19c).** Yield: 65% (0.195 g from 0.20 g) as a light yellow solid; m.p. 184-190 °C; R_f = 0.62 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm)$^{-1}$ = 1709 (CO_2CH_3), 1605 (C=N), 742 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.94 (s, 3H, OCH_3Ar), 4.08 (s, 3H, CO_2CH_3), 4.25 (s, 3H, NCH_3), 7.14 (dd, J_1 = 9.0, J_2 = 2.4 Hz, 1H, ArH), 7.39–7.46 (m, 2H, ArH), 7.59 (d, *J* = 8.4 Hz, 1H, ArH), 7.70 (t, *J* = 7.6 Hz, 1H, ArH), 8.01 (d, *J* = 9.0 Hz, 1H, ArH), 8.24 (d, *J* = 7.8 Hz, 1H, ArH), 8.95 (s,1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 34.8, 53.0, 56.0, 104.0, 110.8 116.0, 118.3, 121.4, 121.7, 124.3, 129.6, 132.4, 135.7, 136.2, 136.7, 138.0,

144.0, 148.5 158.4, 165.9, 166.2 ppm; HRMS (ESI) m/z: calcd. for $C_{22}H_{17}N_3O_3S$ [M + H^+]: 404.1069, found: 404.1058.

Methyl 1-(5,6-dimethoxybenzo[*d*]thiazol-2-yl)-9-methyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (19d). Yield: 55% (0.18 g from 0.20 g) as a brown solid; m.p. 220-222 °C; R_f = 0.62 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1702 (CO_2CH_3), 1618 (C=N), 726 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.01 (s, 6H, $(OCH_3)_2Ar$), 4.07 (s, 3H, CO_2CH_3), 4.21 (s, 3H, NCH_3), 7.38 (t, *J* = 7.32 Hz, 2H, ArH), 7.53–7.56 (m, 2H, ArH), 7.67 (t, *J* = 7.8 Hz, 1H, ArH), 8.20 (d, *J* = 7.8 Hz, 1H, ArH), 8.90 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 34.7, 53.0, 56.2, 56.5, 102.4, 105.0, 110.7, 118.2, 121.3, 121.7, 128.9, 129.5, 131.0, 132.3, 135.8, 136.1, 136.6, 143.9, 148.3, 149.2, 149.5, 166.1, 166.3 ppm; HRMS (ESI) m/z: calcd. for $C_{23}H_{19}N_3O_4S$ [M + Na^+]: 456.0994, found: 456.0992.

Methyl 1-(5,6-dimethylbenzo[*d*]thiazol-2-yl)-9-methyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (19e). Yield: 56% (0.17 g from 0.20 g) as a yellow solid; m.p. 170-175 °C; R_f = 0.73 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1702 (CO_2CH_3), 1620 (C=N), 736 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$), δ = 2.45 (s, 6H, $(CH_3)_2Ar$), 4.08 (s, 3H, CO_2CH_3), 4.20 (s, 3H, NCH_3), 7.41 (t, *J* = 7.4 Hz, 1H, ArH), 7.58 (d, *J* = 8.3 Hz, 1H, ArH), 7.70 (t, *J* = 7.5 Hz, 1H, ArH), 7.77 (s, 1H, ArH), 7.91 (s, 1H, ArH), 8.25 (d, *J* = 7.7 Hz, 1H, ArH), 8.96 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.4, 20.5, 34.7, 53.0, 110.8, 118.4, 120.8, 121.4, 121.8, 123.9, 129.0, 129.6, 132.4, 133,7, 134.0, 135.7, 135.9, 136.3, 136.7, 144.0, 152.7, 166.2, 167.0 ppm; HRMS (ESI) m/z: calcd. for $C_{23}H_{19}N_3O_2S$ [M + Na^+]: 424.1096, found: 424.1052.

Methyl 9-methyl-1-(6-methylbenzo[*d*]thiazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (19f). Yield: 50% (0.14 g from 0.20 g) as a yellow solid; m.p. 198-200 °C; R_f = 0.71 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1707 (CO_2CH_3), 1624 (C=N), 731 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.55 (s, 3H, CH_3Ar), 4.09 (s, 3H, CO_2CH_3), 4.22 (s, 3H, NCH_3), 7.35 (dd, J_1 = 8.3, J_2 = 1.4 Hz, 1H, ArH), 7.39–7.45 (m, 1H, ArH), 7.59 (d, *J* = 8.4 Hz, 1H, ArH), 7.68–7.72 (m, 1H, ArH), 7.81 (m, 1H, ArH), 8.02 (d, *J* = 8.3 Hz, 1H, ArH), 8.23–8.25 (m, 1H, ArH), 8.96 (s, 1H, ArH) ppm; ^{13}C (125 MHz, $CDCl_3$) δ = 21.8, 34.7, 53.0, 110.7, 118.4, 121.3, 121.4, 121.6, 121.7, 123.2, 128.0, 129.7, 132.4, 135.7, 136.2, 136.3, 136.7, 144.1, 152.1, 166.2, 167.3 ppm; HRMS (ESI) m/z: calcd. for $C_{22}H_{17}N_3O_2S$ [M + H^+]: 388.1120, found: 388.1110.

Methyl 1-(4,6-dimethylbenzo[*d*]thiazol-2-yl)-9-methyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (19h). Yield: 52% (0.16 g from 0.20 g) as a yellow solid; m.p. 178-180 °C; R_f = 0.73 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1702 (CO_2CH_3), 1610 (C=N), 733 (C-S), ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.49 (s, 3H, CH_3Ar), 2.78 (s, 3H, CH_3Ar), 4.08 (s, 3H, CO_2CH_3), 4.28 (s, 3H, NCH_3), 7.15 (s, 1H, ArH), 7.40 (t, *J* = 7.5 Hz, 1H, ArH), 7.57 (d, *J* = 8.4 Hz, 1H, ArH), 7.62 (s, 1H, ArH), 7.69 (t, *J* = 7.7 Hz, 1H, ArH), 8.22 (d, *J* =7.8 Hz, 1H, ArH), 8.93 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 18.6, 21.8, 35.0, 52.9, 110.7, 118.3, 119.0, 121.3, 121.7, 128.5, 129.5, 131.0, 132.4, 133.0, 135.8, 136.0, 136.1, 136.5, 136.6, 143.9, 151.6. 166.2, 167.9 ppm; HRMS (ESI) m/z: calcd. for $C_{23}H_{19}N_3O_2S$ [M + H^+]: 402.1276, found: 401.1255.

Methyl 9-benzyl-1-(5,6-dimethoxybenzo [*d*]thiazol-2-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (23d). Yield: 76% (0.17 g from 0.15 g) as a yellow solid; m.p. 180-182 °C; R_f = 0.64 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1709 (CO_2CH_3), 1620 (C=N), 732 (C-S); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.95 (s, 3H, OCH_3Ar), 3.99 (s, 3H, OCH_3Ar), 4.07 (s, 3H, CO_2CH_3), 6.23 (s, 2H, CH_2Ar), 6.73 (d, *J* = 7.1 Hz, 2H, ArH), 7.04–7.08 (m, 2H, ArH), 7.09–7.12 (m, 1H, ArH), 7.21 (s, 1H, ArH), 7.31 (s, 1H, ArH), 7.40–7.43 (m, 1H, ArH), 7.55 (d, *J* = 8.3 Hz, 1H, ArH), 7.62–7.65 (m, 1H, ArH), 8.27 (d, *J* = 7.8 Hz, 1H, ArH), 8.96 (s, 1H, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 50.0, 53.0, 56.2, 56.4, 102.3, 104.8, 111.4, 118.1, 121.7, 121.8, 126.1, 127.1, 128.5, 129.1, 129.7, 133.0, 135.7, 136.3, 137.1, 137.7, 144.0, 148.1, 149.2, 149.4, 166.1 ppm; HRMS (ESI) m/z: calcd. for $C_{29}H_{23}N_3O_4S$ [M + H^+]: 510.1088, found: 510.1067.

3-(6-Ethyl-6*H*-thiazolo[4,5-*c*]carbazol-2-yl)-9-methyl-9*H*-pyrido[3,4-*b*]indole-1-carbaldehyde (27). Yield: 58% (0.94 g from 0.10) as a greenish solid; m.p. 200-204 °C; R_f = 0.63 (hexane/EtOAc, 75:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1692 (CHO), 1621 (C=N), 731 (C-S); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.53 (t, *J* = 7.2 Hz, 3H, NCH_2CH_3). 4.36 (s, 3H, CO_2CH_3), 4.53 (q, *J* = 7.3 2H, NCH_2CH_3), 7.43–7.46 (m, 2H, ArH), 7.57 (t, *J* = 7.4 Hz, 2H, ArH), 7.60–7.62 (m, 1H, ArH), 7.63–7.66 (m, 1H, ArH), 7.71–7.74 (m, 1H, ArH), 8.23–8.30 (m, 3H, ArH), 8.80 (s, 1H, ArH), 10.34 (s, 1H, CHO) ppm; ^{13}C NMR (125 MHz,$CDCl_3$) δ = 14.3, 38.2, 38.3, 108.5, 109.1, 109.2, 109.8, 110.7, 110.11, 119.9, 120.0, 120.7, 121.2, 121.6, 122.0, 122.6, 122.8, 130.0, 137.4, 137.5, 137.6, 137.7, 151.9, 173.9, 193.6 ppm; HRMS (ESI) m/z: calcd. for $C_{28}H_{20}N_4OS$ [M + Na^+]: 483.1256, found: 483.1218.

2-(1-(4-Bromophenyl)-9-ethyl-9*H*-pyrido[3,4-*b*]indol-3-yl)-6-ethyl-6*H*-thiazolo[4,5-*c*]carbazole. (**26a**) Yield: 75% (0.18 g from 0.15) as a Brown solid; m.p. more than 250 °C; R_f = 0.74 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1619 (C=N), 742 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.03 (t, *J* = 7.1 Hz, 3H, $NCH_2CH_{3Carbazole}$), 1.51 (t, *J* = 7.2 Hz, 3H, NCH_2CH_3), 4.08 (q, *J* = 7.1 Hz, 2H, $NCH_2CH_{3Carbazole}$), 4.49 (q, *J* = 7.2 Hz, 2H, NCH_2CH_3), 7.33–7.36 (m, 1H, ArH), 7.37–7.39 (m, 1H, ArH), 7.48 (d, *J* = 8.3 Hz, 1H, ArH), 7.51–7.53 (m, 2H, ArH), 7.58–7.60 (m, 2H, ArH), 7.61–7.62 (m, 1H, ArH), 7.63–7.66 (m, 1H, ArH), 7.78–7.80 (m, 2H, ArH), 8.22–8.25 (m, 2H, ArH), 8.32 (d, *J* = 7.8 Hz, 1H, ArH), 9.11 (s, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.1, 14.2, 38.1, 38.6, 108.0, 109.0, 110.5, 110.9, 111.0, 115.9, 119.6, 120.6, 121.7, 122.2, 122.3, 125.5, 128.4, 128.8, 128.9, 129.5, 129.6, 131.6, 135.6, 137.5 139.8, 141.3, 142.6, 143.9, 149.3, 167.8 ppm; HRMS (ESI) m/z: calcd. for $C_{34}H_{25}BrN_4S$ [M + H^+]: 601.1062, found: 601.1035.

2-(9-Methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)thiazolo[4,5-*b*]pyridine (5m). Yield: 40% (0.06 g from 0.10) as a light blue solid; m.p. 165-167 °C; R_f = 0.61 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1622 (C=N), 740 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.25 (s, 3H, NCH_3). 7.07–7.10 (m, 1H, ArH), 7.33 (t, *J* = 7.4 Hz, 1H, ArH), 7.54 (d, *J* = 8.2 Hz, 1H, ArH), 7.66 (t, *J* = 7.6 Hz, 1H, ArH), 7.76–7.80 (m, 1H, ArH), 8.13–8.15 (m, 2H, ArH), 8.39–8.43 (m, 1H, ArH), 8.45 (d, *J* = 8.2 Hz, 1H; ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 35.0, 110.4, 110.5, 114.0, 117.8, 119.8, 120.5, 121.4, 121.5, 129.4, 133.1, 134.0, 136.7, 138.4, 144.0, 148.4, 151.8, 164.2 ppm; HRMS (ESI) m/z: calcd. for $C_{18}H_{12}N_4S$ [M + H^+]: 317.086, found: 317.0832.

Methyl 1-(benzo[*d*]thiazol-2-yl)-9-ethyl-9H-pyrido[3,4-*b*]indole-3-carboxylate (**20n**). Yield: 72% (0.20 g from 0.20 g) as a light yellow solid; m.p. 200-202 °C; R_f = 0.68 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1709 (CO_2CH_3), 1615 (C=N), 738 (C-S); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.34 (t, *J* = 7.1 Hz, 3H, NCH_2CH_3). 4.09 (s, 3H, CO_2CH_3), 5.06 (q, *J* = 7.1 Hz, 2H, NCH_2CH_3), 7.41–7.44 (m, 1H, ArH), 7.46–7.50 (m, 1H, ArH), 7.53–7.56 (m, 1H, ArH), 7.63 (d, *J* = 8.3 Hz, 1H, ArH), 7.70–7.72 (m, 1H, ArH), 8.03 (d, *J* = 7.7 Hz, 1H, ArH), 8.13 (d, *J* = 8.0 Hz, 1H,ArH), 8.26 (d, *J* = 7.8 Hz, 1H, ArH), 8.98 (s, 1H, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 15.0, 41.5, 53.0, 110.9, 118.6, 121.4, 121.7, 121.8, 121.9, 123.7, 125.9, 126.3, 129.6, 132.9, 135.1, 135.6, 142.9, 154.0, 166.1, 168.9 ppm; HRMS (ESI) m/z: calcd. for $C_{22}H_{17}N_3O_2S$ [M + H^+]: 390.1276, found: 390.1245.

6-(9-Methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-[1,3]dioxolo[4',5':4,5]benzo[1,2-*d*]thiazole (5l). Yield: 65% (0.22 g from 0.20 g) as a yellow solid; m.p. 208-210 °C; R_f = 0.66 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1630 (C=N), 743 (C-S); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.18 (s, 3H, NCH_3), 6.10 (s, 2H, $(O)_2CH_2$)Ar), 7.34 (t, *J* = 7.42 Hz, 1H, ArH), 7.37 (s, 1H, ArH), 7.53 (s, 1H, ArH), 7.54 (d, *J* = 8.4 Hz, 1H, ArH), 7.66 (t, *J* = 7.6 Hz, 1H, ArH), 8.05 (d, *J* = 4.9 Hz, 1H, ArH), 8.17 (d, *J* = 7.8 Hz, 1H, ArH), 8.53 (d, *J* = 4.9 Hz, 1H, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 34.7, 100.5, 101.9, 103.0, 110.5, 115.7, 120.4, 121.1, 121.5, 129.1, 129.8, 132.3, 135.0, 136.1, 138.3, 143.9, 147.4, 148.0, 149.1, 167.6 ppm; HRMS (ESI*)* m/z: calcd. for $C_{20}H_{13}N_3O_2S$ [M + H^+]: 360.081, found: 360.080.

(*E*)-9-ethyl-*N*-((9-methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)methylene)-9*H*-carbazol-3-amine (29). Yield: 97% (0.37 g from 0.20 g) as a yellow solid; m.p. 180-182 °C; R_f = 0.41 (hexane/EtOAc, 70:30, v/v); IR (neat): ν_{max} (cm^{-1}) = 1623 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.48 (t, *J* = 7.2 Hz, 3H, NCH_2CH_3). 4.31 (s, 3H, NCH_3), 4.42 (q, *J* = 7.2 Hz, 2H, NCH_2CH_3), 7.28–7.36 (m, 2H, ArH), 7.44 (d, *J* = 8.2 Hz, 1H, ArH), 7.47–7.52 (m, 2H, ArH), 7.57 (d, *J* = 8.3 Hz, 1H, ArH), 7.64–7.69 (m, 2H, ArH), 8.07 (d, *J* = 4.9 Hz, 1H, ArH), 8.14 (d, *J* = 7.7 Hz, 1H, ArH), 8.19 (d, *J* = 7.8 Hz, 1H, ArH), 8.22 (d, *J* = 2.0 Hz, 1H, ArH), 8.62 (d, *J* = 4.9 Hz, 1H, ArH), 9.29 (s, 1H, CH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 14.0, 35.0, 37.8, 108.8, 109.0, 110.2, 113.1, 115.7, 119.2, 120.2, 120.3, 120.7, 121.2, 121.5, 123.2, 123.7, 126.1, 129.0, 131.8, 136.4, 138.7, 139.3, 139.8, 140.7, 143.1, 143.5, 157.2 ppm; HRMS (ESI) m/z: calcd. for $C_{27}H_{22}N_4$ [M + H^+]: 403.1923, found: 403.1911.

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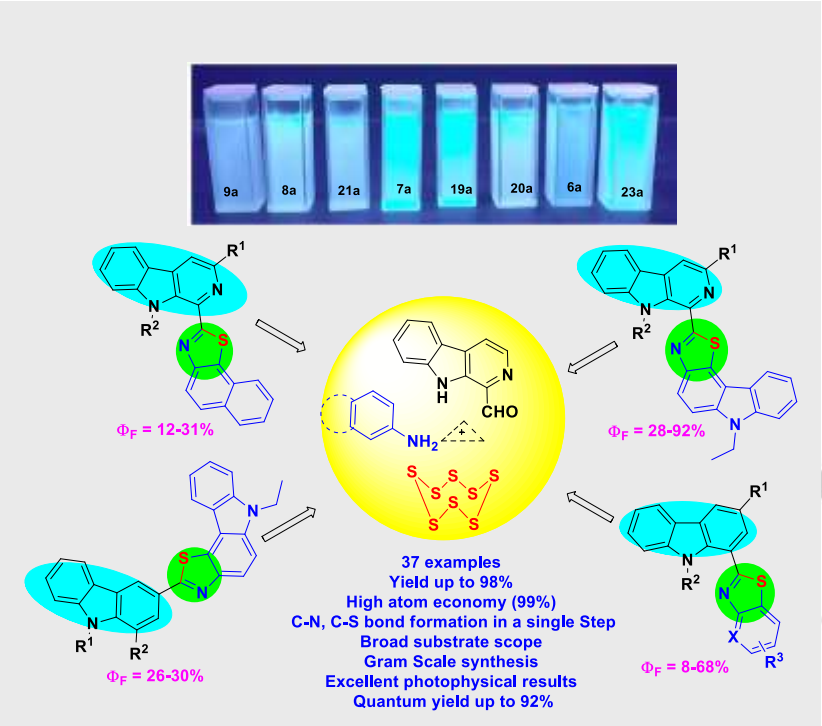
1. D. J. Newman, G. M. Cragg, *J. Nat. Prod*. **2012**, *75*, 311-335; b) D. J. Newman, G. M. Cragg, *J. Nat. Prod*. **2007**, *70*, 461-477; c) D. J. Newman, G. M. Cragg, K. M. Snader, *J. Nat. Prod*. **2003**, *66*, 1022-1037; d) R. Cao, W. Peng, Z. Wang, A. Xung, *Curr. Med. Chem*. **2007**, *14*, 479-500; e) N. Devi, S. Kumar, S. K. Pandey and V. Singh, *Asian J. Org. Chem.* **2018**, *7*, 6-36.
2. a) L. He, Y. Li, C.-P. Tan, R.-R. Ye, M.-H. Chen, J.-J. Cao, L.-N. Ji, Z.-W. Mao, *Chem. Sci.* **2015**, *6*, 5409-5418; b) G. Nenaah, *Fitoterapia* **2010**, *81*, 779-782; c) H. Chen, P. Gao, M. Zhang, W. Liao, J. Zhang, *New J. Chem.* **2014**, *38*, 4155-4166; d) Y. H. Wang, J. G. Tang, R. R. Wang, L. M. Yang, Z. J. Dong, L. Du, X. Shen, J. K. Liu, Y. T. Zheng, *Biochem. Biophys. Res. Commun*. **2007**, *355*, 1091-1095; e) Y. C. Maksay, M. Simonyi, *Eur. J. Pharmacol*. **1985**, *117*, 275-278; f) T. P. Hamsa, G. Kuttan, *Eur. J. Pharmacol*. **2010**, *649*, 64-73; g) A. Daugan, P. Grondin, C. Ruault, A. C. L. M. Gouville, H. Coste, J. Kirilovsky, F. Hyafil, R. Labaudiniere, *J. Med. Chem*. **2003**, *46*, 4533-4542; h) S. Wang, K. Fang, G. Dong, S. Chen, N. Liu, Z. Miao, J. Yao, J. Li, W. Zhang, C. Sheng, *J. Med. Chem*. **2015**, *58*, 6678-6696; i) A. S. Gothelf, K. V. Gothelf, R. G. Hazell, K. A. Jorgensen, *Angew. Chem. Int. Ed.* **2002**, *41*, 4236-4238; j) S. Kumar, A. Singh, K. Kumar, V. Kumar, *Eur. J. Med. Chem*. **2017**, *142*, 48-73; k) X. Huo; W. Li, B. Zhang, X. Chen, Y. Zhou, J. Zhang, X. Han and B. Dai, *Chin. J. Org. Chem.*, **2018**, *38*, 3356-3362; l) H. Gu, N. Li, J. Dai, Y. Xi, S. Wang, J. Wang, *Int. J. Mol. Sci.* **2018**, *19*, 3179-3195.
3. a) M. A. Abdelsalam, O. M. A. Wafa, E. A. Badawey, M. S. E. Shoukrofy, M. M. E. Miligy, N. Gouda, *Future. Med. Chem*. **2018**, *24*, 2791-2814; *b*) A. Carvalho, J. Chu, C. Meinguet, R. Kiss, G. Vandenbussche, B. Masereel, J. Wouters, A. Kornienko, J. Pelletier, V. Mathieu, *Eur J Pharm.* **2017**, *805*, 25-35; c) H. Du, H. Gu, N. Li, J. Wang, *Med. Chem. Commun.* **2016**, ***7***, 636-645; d) S. U. Dighe, S. Khan, I. Soni, P. Jain, S. Shukla, R. Yadav, P. Sen, S. M. Meeran, S. Batra, *J. Med. Chem.* **2015**, *58*, 3485-3499.
4. L. A. Sorbera, L. Martin, P. A. Leeson, J. Castaner, *Drugs Future*, **2001**, *26*, 15-19.
5. a) A. Das, S. U. Dighe, N. Das, S. Batra, P. Sen, *Spectrochim. Acta Part A.* **2019**, *220*, 1-18; b) S. Swami, D. Behera, A. Agarwala, V. P. Verma, R. Shrivastava, *New J. Chem.* **2018**, *42*, 10317-10326.
6. a) C. Piemontesi, Q. Wang, J. Zhu, *J. Am. Chem. Soc.* **2016**, *138*, 11148-11151; b) D. Chandrasekhar, S. Borra, J. S. Kapure, G S. Shivaji, G. Srinivasulu, R. A. Maurya, *Org. Chem. Front.* **2015**, *2*, 1308-1312; c) E. Xie, A. Rahman, X. Lin, *Org. Chem. Front.* **2017**, *4*, 1407-1410.
7. a) N. P. Prajapati, R. H. Vekariya, M. A. Borad, H. D. Patel, *RSC Adv*. **2014**, *4*, 60176-60208; b) G. Li, H. Xie, J. Chen, Y. Guo, G. J. Deng, *Green Chem.* **2018**, *20*, 827-831.
8. a) K. Serdons, C. Terwinghe, P. Vermaelen, K. V. Laere, H. Kung, L. Mortelmans, G. Bormans, A. Verbruggen, *J. Med. Chem*. **2009**, *52*, 1428-1437; b) C. Praveen, A. N. Kumar, P. D. Kumar, D. Muralidharan, P. T. Perumal, *J. Chem. Sci.* **2012**, *124*, 609-624; c) X. Su, N. Vicker, D. Ganeshapillai, A. Smith, A. Purohit, M. J. Reed, B. V. L. Potter, *Mol. Cell. Endocrinol.* **2006**, *248*, 214-217; d) T. D. Bradshaw, A. D. Westwell, *Curr. Med. Chem*. **2004**, *11*, 1009-1021; e) S. T. Huang, I. J. Hsei, C. P. Chen, *Bioorg.Med.Chem*. **2006**, *14*, 6106-6119; f) R. K. Gill, R. K. Rawal, J. Bariwal, *Arch. Pharm. Chem. Life Sci.* **2015**, *348*, 155-178.
9. a) P. Hrobarik, P. Zahradnik, W. M. F. Fabian, *Phys. Chem. Chem. Phys*. **2004**, *6*, 495–502; b) F. Lu, R. Hu, S. Wang, X. Guo, G. Yang, *RSC. Adv*. **2017**, *7*, 4196–4202; c) K. Wang, Q. Lv, Y. Chen, H. Chen , Z. Liu, D. Cao, Qi. Fang, *Spectrochim. Acta Part A*. **2016**, *153*, 669-673.
10. a) V. Hrobarikova, P. Hrobarik, P. Gajdos, I. Fitilis, M. Fakis, P. Persephonis, P. Zahradnık, *J. Org. Chem*. **2010**, *75*, 3053-3068; b) M Zajac, P. Hrobarik,. P. Magdolen, P. Foltinova, P. Zahradnik, *Tetrahedron.* **2008**, *64*, 10605-10618.
11. V. Kumar, D. Singh, A. K. Paul, R. Shrivastava, V. Singh, *New J. Chem.* **2019**, **43**, 18304-18315.
12. a) P. Beletskaya, V. P. Ananikov, *Chem. Rev*. **2011**, *111*, 1596-1636; b) H. Liu, X. Jiang, *Chem. Asian J.* **2013**, *8*, 2546-2563; c) C. Shen, P. Zhang, Q. Sun, S. Bai, T. S. Andy Hor, X. Liu, *Chem. Soc. Rev.* **2015**, *44*, 291-314; d) C. Zhang, J. McClure, C. J.Chou, *J. Org. Chem.* **2015**, *80*, 4919-4927; e) S. R. Guo, W. M. He, J. N. Xiang, Y. Q. Yuan, *Chem. Commun.* **2014**, *50*, 8578-8581; f) X. Zhu, X. Xie, P. Li, J. Guo, L. Wang, *Org. Lett.* **2016**, *18*, 1546-1549; g) E. Schaumann, *Top. Curr. Chem.* **2007**, *274*, 1-34; h) F. L. Yang, S. K. Tian, *Angew. Chem. Int. Ed.* **2013**, *52*, 4929-4932; k) Z. Y. Gu, J. J. Cao, S. Y. Wang, S. J. Ji, *Chem. Sci*. **2016**, *7*, 4067-4072; i) P. Zhao, Y. Liu, C. Xi, *Org. Lett.* **2015**, *17*, 4388-4391; j) P.Sang, Z. Chen, J. Zou, Y. Zhang, *Green Chem*. **2013**, *15*, 2096-2100; k) A. Dey, A. Hajra *Org. Lett*. **2019**, *21*, 1686-1689.
13. a) T. B. Nguyen, L. Ermolenko, P. Retailleau, A. A. Mourabit, *Angew. Chem. Int. Ed*. **2014**, *53*, 13808-13812; b) T. B. Nguyen, L. Ermolenko, W. A. Dean, A. A. Mourabit, *Org. Lett.* **2012**, *14*, 5948-5951; c) T. B. Nguyen, K. Pasturaud, L. Ermolenko, A. A. Mourabit, *Org. Lett.* **2013**, *15*, 4218-4221; d) T. B. Nguyena, P. Retailleaua, *Adv. Synth. Catal.* **2017**, *21*, 3843-3847; (*e*) T. B. Nguyen, *Adv. Synth. Catal.* **2017**, *359*, 1006-1130; f) T. B. Nguyen, P. Retailleau, *Green Chem.* **2018**, *20*, 387-390; g) T. B. Nguyen, *Asian J. Org. Chem.* **2017**, *6*, 477-491; h) T. B. Nguyen, K. Pasturaud, L. Ermolenko, A. Al-Mourabit, *Org. Lett.* **2015**, *17*, 2562-2565.
14. a) X. Che, J. Jiang, F. Xiao, H. Huang, G. –J. Deng, *Org. Lett.* **2017**, *19*, 4576-4579; b) G. Li, H. Xie, J. Chen, Y. Guo, G. –J. Deng, *Green Chem.* **2017**, *19,* 4043-4047; c) H. Xie, G. Li. F. Zhang, F. Xiao, G. –J. Deng, *Green Chem.* **2018**, *20*, 827-831. d) Q. Xing, Y. Ma, H. Xie, F. Xiao, F. Zhang, G. –J. Deng, *J. Org. Chem*. **2019**, *84*, 1238-1246.
15. a) D. Singh, V. Kumar, N. Devi, C. C. Malakar, R. Shankar, V. Singh *Adv. Synth. Catal*. **2017**, *359*, 1213-1226; b) D. Singh, S. K. Tiwari, V. Singh *New J. Chem.* **2019**, *43*, 93-102; c) D. Singh, N. Devi, V. Kumar, C. C. Malakar, S. Mehra, S. Rattan, R. K. Rawal,

V. Singh, *Org. Biomol. Chem.* **2016**, *14*, 8154-8166; d) D. Singh, P. Sharma, R. Kumar, S. K. Pandey, C. C. Malakar, V. Singh, *Asian J. Org. Chem.* **2018**, *7*, 383-394.

16. M. K. Bera, S. K. Samanta, *Org. Biomol. Chem.* **2019**, *17*, 6441-6449. b) P. N. Reddy, B. V. S. Reddy, P. Padmaja, *Curr. Org. Synth.* **2018**, *15*, 815-838; b) A. Monga, S. Bagchi, A. Sharma, *New J. Chem.* **2018**, *42*, 1551-1576; c) P. T. Parvatkar, P. S. Parameswaran, S. G. Tilve, *Chem. – Eur. J.* **2012**, *18*, 5460-5489; c) Y. M. Ren, C. Cai, R. C. Yang, *RSC Adv*. **2013**, *3*, 7182-7204.
17. N. Devi, D. Singh, G. Kaur, S. Mor, C C Malakar, V. Singh, *New J. Chem.* **2017**, *41*, 1082-1093.

Layout 2:

FULL PAPER



Fluorescent Materials*

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Iodine Catalysed Expeditious Synthesis of Highly Fluorescent β-Carboline C-1(3) Tethered Thiazolo[4,5-*c*]carbazole, Naphtho[2,1-*d*]thiazole and Benzothiazole Derivatives and Estimation of their Light Emitting

This methodology provides an easy access to gram scale synthesis of highly fluorescent β-carboline tethered thiazolo[4,5-*c*]carbazoles and benzothiazole derivatives in excellent yields. The synthesized analogues may find wide application in medicinal chemistry with potential scope as anticancer agents or DNA staining agents and in material science as fluorescent probes and chemosensors.