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Et_3N-DMSO Supported One-pot Synthesis of Highly Fluorescent β-Carboline Linked Benzothiophenones *via* Sulphur Insertion and Estimation of Their Photophysical Properties

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Abstract

A robust transition metal-free strategy is presented to access novel β-carboline tethered benzothiophenone derivatives from 1(3)-formyl-β-carbolines using elemental sulphur activated by Et_3N/DMSO. This expeditious catalyst-free reaction proceeds through the formation of β-carboline based 2-nitrochalcones followed by incorporation of sulphur to generate the multifunctional β-carboline linked benzothiophenones in good to excellent yields. The synthetic strategy can also be extended towards the synthesis of β-carboline linked benzothiophenes. Moreover, the products as afforded thereof emerged as promising fluorophores and displayed excellent light-emitting properties with quantum yield (Φ_F) upto 47%.

Keywords

β-Carboline; Metal-free; Sulphur insertion; Benzothiophene; Photophysical properties

Introduction

Pyrido[3,4-*b*]indole moiety, commonly referred as β-carboline, is the core unit of about one quarter of natural products [1] and pharmacologically active compounds endowed with anticancer [2], anti-inflammatory, antioxidant, antimalarial, antifungal, and anti-leishmanial activities [3] (Figure 1). Notably, this privileged scaffold is incorporated by several marketed drugs like Abecarnil, Tadalafil, Cipargamin, Yohimbine etc. which are used in the treatment of various ailments [4]. Apart from their pharmaceutical properties; β-carboline derivatives also find various applications such as organocatalysts, ligands and fluorescent probes [5]. Importantly, β-carbolines are also used as fluorescence standards. Recently, a novel β-carboline-based fluorescent chemosensor was developed by Batra and co-workers for quantitative analysis of fluoride ions (F^-) at PPB level [6].

Sulphur-containing organic compounds are broadly associated with numerous bioactive natural products and pharmaceutical drugs [7]. Thioaurones (2-benzylidene benzo[*b*]thiophen-3(2*H*)-one) are sulphur containing heterocyclic compounds, an important subclass of flavonoids which were first introduced by O’ Sullivan in 1977 [8]. Specifically, thioaurones and their analogues show a variety of biological activities such as anticancer [9], inhibition of tyrosine phosphatase 1B, antioxidant properties etc [10]. Due to their numerous applications, they have found diverse uses such as thioindigo-like dyes, photo-responsive devices and photo-switchable biomolecules [11]. Moreover, these compounds can also be used as synthetic intermediates for various sulphur-containing bioactive molecules [12] (Figure 1).

In our research endeavors, we have been involved in exploration of synthetic potential of 1-formyl-9*H*-β-carboline (An alkaloid, Kumujian C) [13] for preparing chemical libraries of β-carboline substituted [14] and N-fused heterocycles [15] which may be attributed to the versatility of this natural product [1a]. Encouraged by the applications of β-carboline and benzothiophenes motif in medicinal and material chemistry; it was envisaged to construct a β-carboline based novel molecular hybrid containing benzothiophene moiety [16] (Figure 1). In organic synthesis, aromatic compounds having nitro group plays vital role as building block for the synthesis of nitrogen-containing functional groups or aza-heterocyclic frameworks. However, the organic transformations in which aromatic nitro group act as leaving groups are less reported and requires the use of transition metal catalysts such as Cu, Rh, Pd etc. [17]. Though, several elegant methods have been developed for the synthesis of thioaurones but these methods involved the use of organosulphur based substrates [18]. Moreover, these methods are associated with some limitations such as use of costly metal catalysts, air-sensitive starting materials, malodorous sulphides or thiols, low yields and multistep synthesis. To overcome these drawbacks, elemental sulphur as the sulphur source has emerged as a surrogate approach, which is frequently used these days. In this context, several research groups are actively involved in the development of novel and efficient approaches for synthesis of sulphur containing heterocycles [19]. Inspired by the findings of Nguyen and co-workers [20] and as a part of our ongoing project [21], we have devised a simple and efficient one-pot practical approach for the construction of β-carboline tethered benzothiophenone derivatives *via* incorporation of sulphur. To our knowledge, it is first report towards one-pot synthesis of novel β-carboline tethered benzothiophenones and evaluation of their light emitting properties. In this regard, the detailed studies are presented and discussed herein.

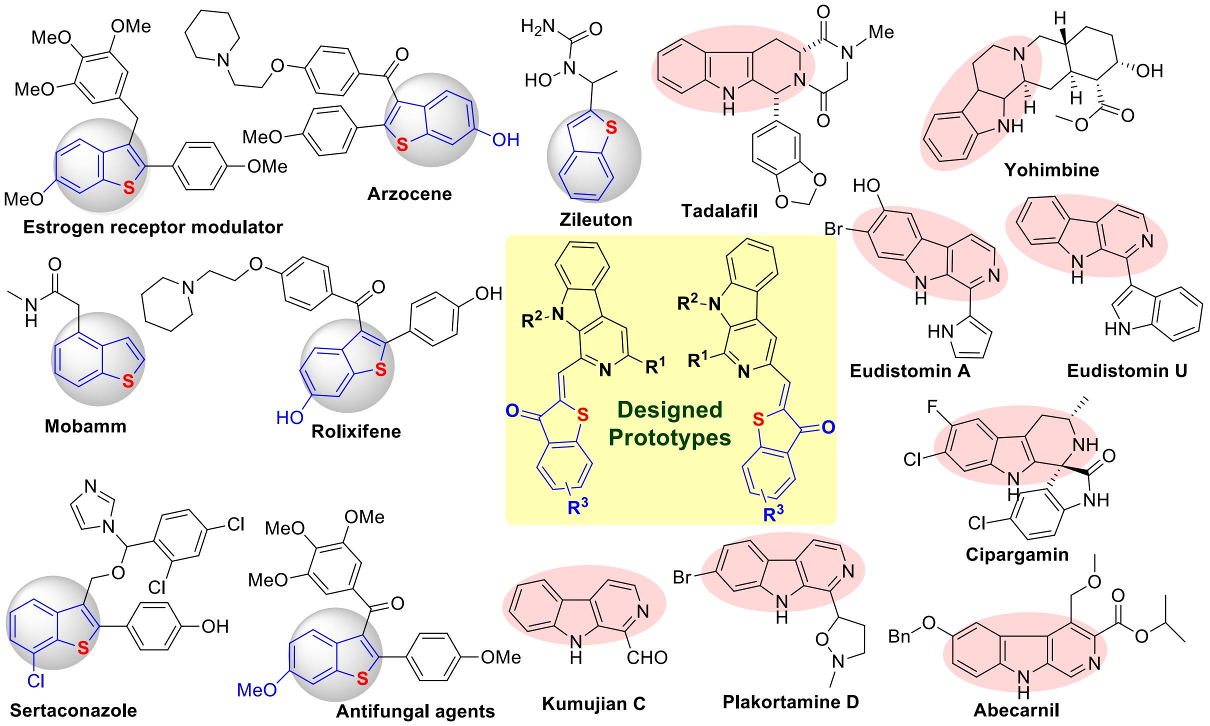
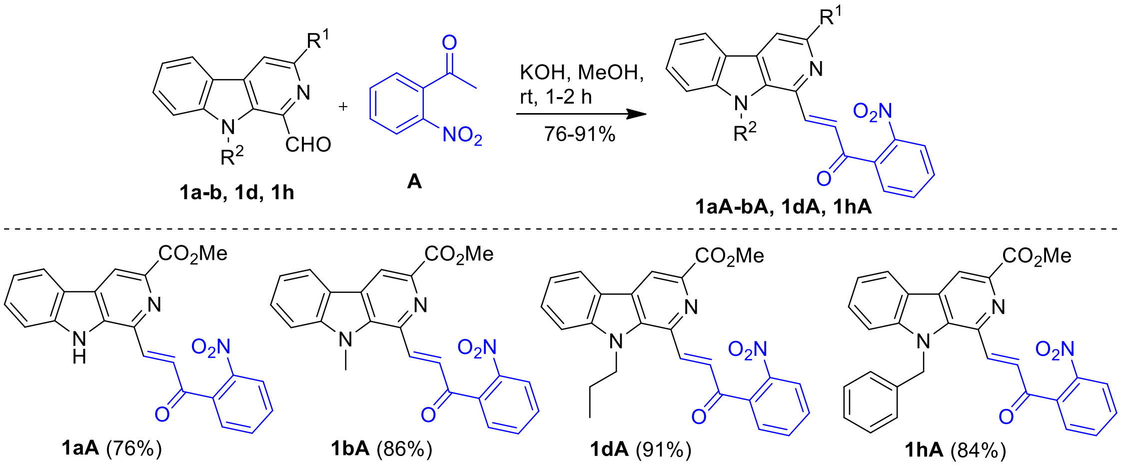


Figure 1: Representative examples of some commercial drugs and biologically active alkaloids.

Results and Discussion

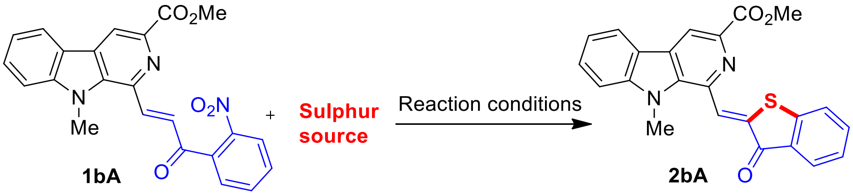
The present study commenced with the synthesis of β-carboline based 2-nitrochalcone **1bA** which was prepared *via* Claisen-Schmidt condensation of 1-formyl-β-carboline **1b** with 2-nitroacetophenone (**A**) in the presence of KOH (1.05



Scheme 1: Synthesis of β-carboline linked 2-nitrochalcones.

equiv.) in dry MeOH at room temperature (Scheme 1). The analytically pure product was obtained in 86% yield by simple filtration of precipitates followed by washing with dry MeOH. With an objective to achieve the synthesis of β-carboline linked benzothiophenone frameworks, we set up screening of conditions for the reaction between β-carboline based 2-nitrochalcone and elemental sulphur by varying different activators (Table 1). Recent findings have revealed that a combination of aliphatic amines with DMSO can activate elemental sulphur for electrophilic addition to generate thioaurones and benzothiophenes [20]. At 70 °C, use of DIPEA in combination with DMF as the solvent was found to be an excellent sulphur activator, leading to the formation of desired product **2bA** in 50% yield after a short silica gel column chromatographic separation (Table 1, entry 1). The structure of **2bA** was confirmed on the basis of spectroscopic data. The ^{1}H-NMR spectrum displayed a singlet for one methine proton at δ 8.69 ppm and the presence of additional nine aromatic protons for β-carboline and benzothiophenone framework indicated the formation of desired product. When elemental sulphur and DIPEA were used in DMSO, a significant increase in the yield (73%) was observed (Table 1, entry 2). At this stage, we realized that DMSO could be a better choice for this transformation as it took lesser time and afforded the product **2bA** in better yield. Then, other amines such as NMP, Et_3N, DBU and DABCO were also investigated. The use of NMP as an activator in DMSO yielded the desired product in 65% yield only (Table 1, entry 3). Interestingly, Et_3N in combination with DMSO at 70 °C offered the anticipated product **2bA** in 78% yields within a short span of 20 min (Table 1, entry 4). The reaction at 90 °C afforded the product **2bA** in 76% yields, however, the same reaction at 30 °C was observed to be sluggish and complete conversion could not be achieved even after 12 h (Table 1, entries 5-6). It was also observed that the reaction in absence of Et_3N failed to generate the anticipated product **2bA** (Table 1, entry 7) which supported the importance of amine/base with DMSO as an activator. Potassium ethylxanthate [22] and sodium sulphide as a sulphur source in the presence of Et_3N in DMSO (Table 1, entries 8-9) also could not furnish the desired product **2bA**.

Table 1: Optimisation of reaction conditions[a]



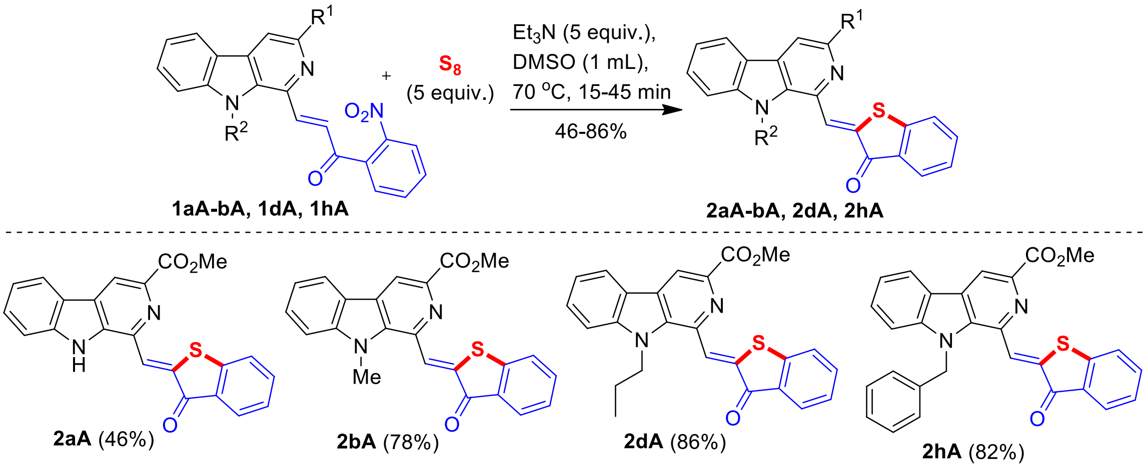
Entry	Base[b]	S Source	Solvent[c]	Temp (°C)	Time	Yields[d] % of 2bA
1	DIPEA	S_8	DMF	70	1 h	50
2	DIPEA	S_8	DMSO	70	45 min	73
3	NMP	S_8	DMSO	80	1 h	65
4	Et_3N	S_8	DMSO	70	20 min	78
5	Et_3N	S_8	DMSO	90	18 min	76
6	Et_3N	S_8	DMSO	30	12 h	45
7[e]	-	S_8	DMSO	90	12 h	NR
8[e]	Et_3N	$C_2H_5OCS_2K$	DMSO	60	10 h	NR
9[f]	Et_3N	Na2S	DMSO	60	20 h	-
10	DABCO	S_8	DMSO	60	20 min	60
11	DBU	S_8	DMSO	70	40 min	30 +

						impurity
12	L-Proline	S_8	DMSO	70	3.5 h	30 + **1bA**
13	Pyridine	S_8	DMSO	70	12 h	NR
14	DMAP	S_8	DMSO	70	3 h	35 + **1bA**
15	Pyrrolidine	S_8	DMSO	60	3 h	40
16[e]	KI	S_8	DMSO	70	2.5 h	NR

[a]All reactions were performed with 0.12 mmol of **1bA**, 0.60 mmol (5.0 equiv.) of sulphur powder and 0.60 mmol (5.0 equiv.) of amine/base in 0.5 mL of solvent; [b]5.0 equiv. of amine/base was used except KI (3.0 equiv.), L-Proline (4.0 equiv.) and DMAP (1.5 equiv.); [c]Dry solvents were used; [d]Isolated yields of the purified product. [e]NR = No reaction was observed; [f]Decomposition of starting material was observed.

The decomposition of product was observed in case of Na_2S. Interestingly, combination of DABCO and DMSO also afforded the desired product *via* a clean reaction within 20 min though only 60% yield was obtained (Table 1, entry 10). The success with DABCO encouraged us to explore other amines like DBU, L-proline, pyridine, DMAP and pyrrolidine as activator but encouraging results were not obtained (Table 1, entries 11-15). Similarly, use of KI as an activator also failed to affect the reaction (Table 1, entry 16). Eventually, we reached the conclusion that combination of Et_3N and DMSO excellently activated the elemental sulphur at 70 °C and was considered the optimal condition for the construction of β-carboline linked benzothiophenone derivatives.

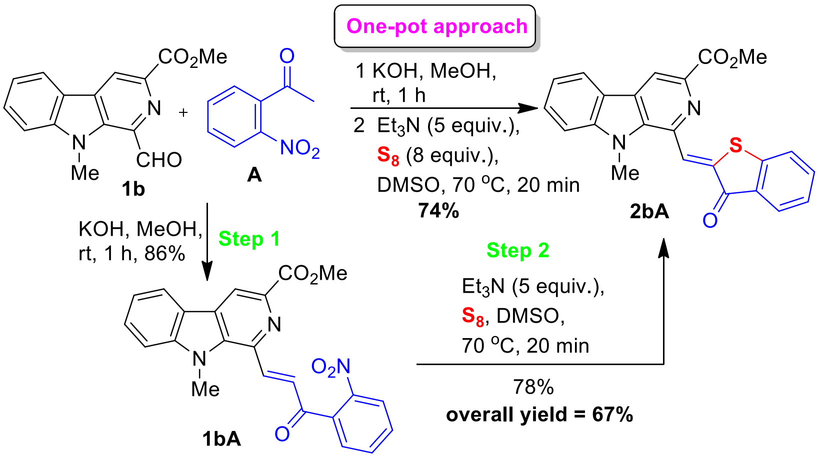
With standardized conditions identified, the scope of this domino approach was investigated with diversely substituted β-carboline based 2-nitrochalcones (**1aA-bA**, **1dA**, and **1hA**) prepared from **1a-b**, **1d** and **1h** in 76-91% yield (Scheme 1). The methodology was found to be general in nature and produced the fluorescent β-carboline linked benzothiophenone derivatives **2aA**-**bA**, **2dA** and **2hA** within 15-45 min in DMSO at 70 °C as depicted in Scheme 2. The analytically pure products were obtained in 46-86% yields after a short silica gel column chromatographic purification.



Scheme 2: Synthesis of β-carboline linked benzothiophenone frameworks.

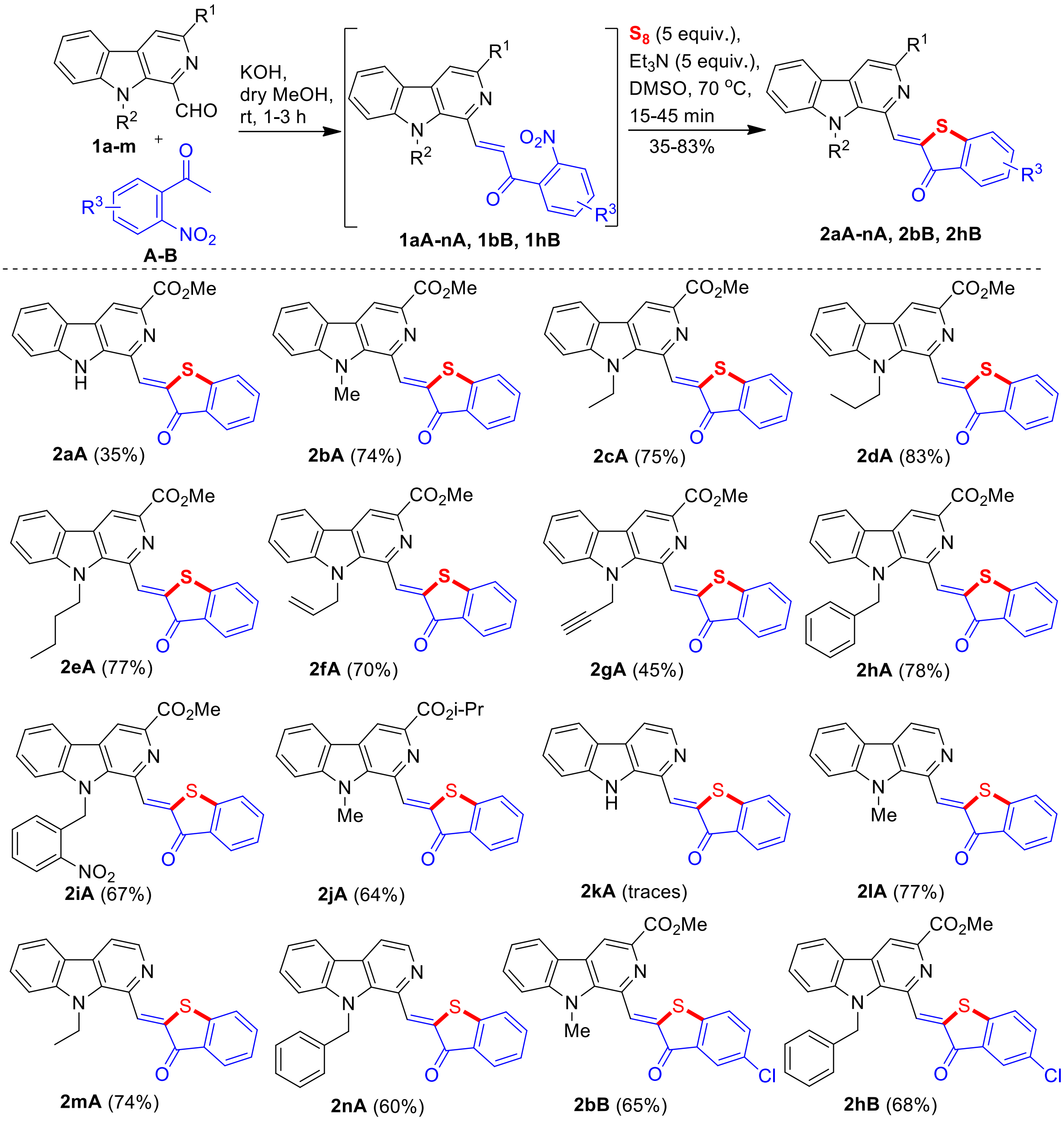
It was observed that *N*-alkyl β-carboline based 2-nitrochalcones (**1bA**, **1dA** and **1hA**) reacted faster and delivered the products (**2bA**, **2dA** and **2hA)** in better yield (78-86%). Conversely, the substrate **1aA** bearing free NH was found to be slow reacting and produced **2aA** in low yield (46%).

From the perspective of green chemistry, one-pot reactions are preferred as less waste is generated; work-up, isolation and purification of intermediates could be avoided [23]. Accordingly, the feasibility of one-pot synthesis of targeted products was attempted. Therefore, after the formation of 2-nitrochalcone **1aA**, excess of MeOH was decanted and the crude product was re-dissolved in 1 mL of DMSO followed by sequential addition of Et_3N (5 equiv.) and elemental sulphur (5 equiv.). To our pleasure, the reaction at 70 °C smoothly afforded the corresponding β-carboline linked benzothiophenone derivative **2bA** in less than 30 min. More importantly, a clean reaction was observed during one-pot strategy which surely avoided the isolation of intermediate (2-nitrochalcone derivative **1bA**) and a significant increment in overall yield of **2bA** (67% to 74%) was also noted (Scheme 3).



Scheme 3: One-pot vs two-step approach for the synthesis of **2bA**.

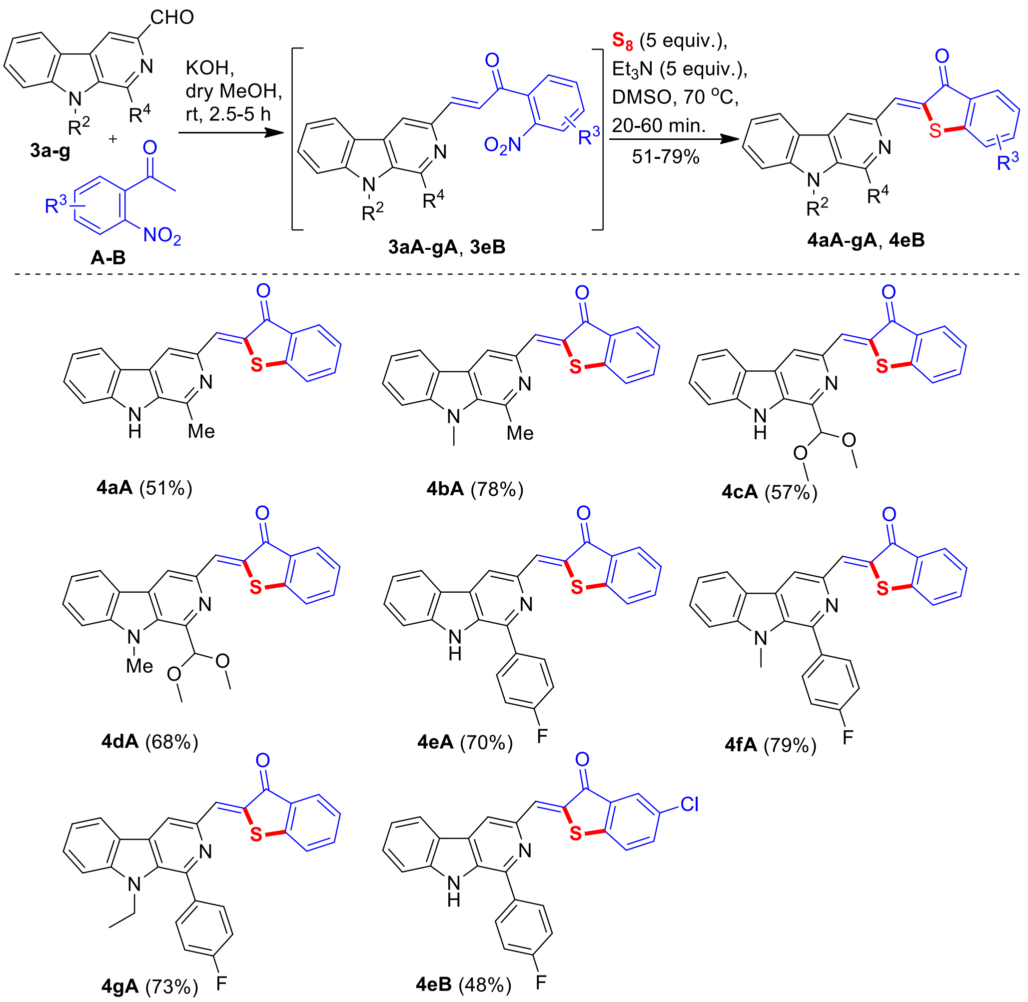
With successful evaluation of one-pot strategy, we next focused our efforts on the generality and scope of this method. Interestingly, diversely substituted 1-formyl-β-carbolines **1a-m** (except **1k**) reacted efficiently with **A-B** under one-pot protocol and furnished the anticipated products (**2aA-nA**, **2bB** and **2hB**) as depicted in Scheme 4.



Scheme 4. One-pot synthesis of β-carboline C-1 tethered benzothiophenone derivatives.

The synthesized products were purified through silica gel column chromatography and further washed with anhydrous methanol to yield the analytically pure products in 35-83% yields (two-step yield). It was observed that *N*-alkyl derivatives (**1bA-jA**, **1lA-nA**, **1bB** and **1hB**) reacted faster and offered the products in higher yields. Next, the substrate **B** bearing chloro substituent took longer reaction times and afforded the targeted products (**2bB** and **2hB**) in slightly lower yields.

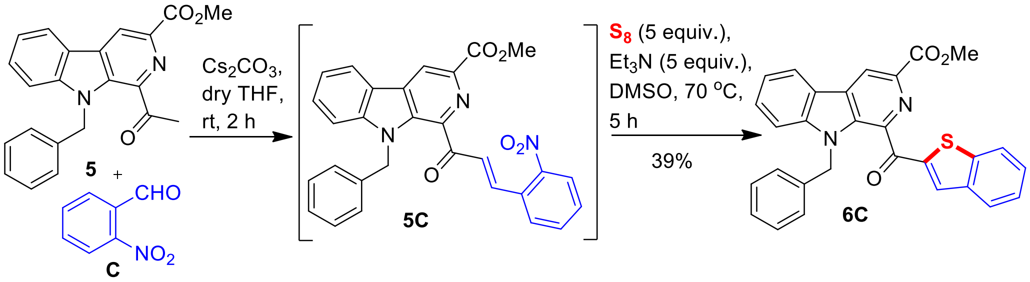
Encouraged by the results obtained from one-pot synthesis of β-carboline C-1 substituted benzothiophenone derivatives, it was sought to extend the scope of this one-pot strategy for the synthesis of β-carboline C-3 tethered benzothiophenones (Scheme 5). The reaction of 3-formyl-9*H*-β-carbolines [14d] (**3a**-**g**) with substituted 2-nitroacetophenones (**A**-**B**) in presence of KOH delivered the corresponding 2-nitrochalcones (**3aA**-**gA** and **3eB**). These *in-situ* generated β-carboline based 2-nitrochalcones were further treated with elemental sulphur and Et_3N in DMSO at 70 ^{o}C which easily afforded the corresponding products (**4aA**-**gA** and **4eB**) in 51-79% yield as presented in Scheme 5. It was observed that the reaction time and yields



Scheme 5. One-pot synthesis of β-carboline C-3 linked benzothiophenone derivatives.

were affected by the nature of substituent at C-1 (R^4) and N-9 (R^2) of β-carboline ring. The substrate bearing dimethoxymethyl group (**3c** and **3d**) reacted smoothly and took lesser reaction time. Similarly, *N*-alkyl (R^2) 3-formyl β-carbolines (**3b**, **3d**, **3f** and **3g**) reacted faster and delivered higher yield as compared to free NH derivatives (**3a**, **3c** and **3e**). In case of **4eB**, slow reaction with low yield was detected due to presence of electron-withdrawing substituents in **B**. Overall, it was noted that the 1-formyl-β-carbolines (**1a-m**) reacted faster and offered the corresponding products in higher yields as compared to 3-formyl-β-carbolines (**3a-g**) which may be attributed to the greater electrophilicity of formyl group at C-1 in β-carboline ring.

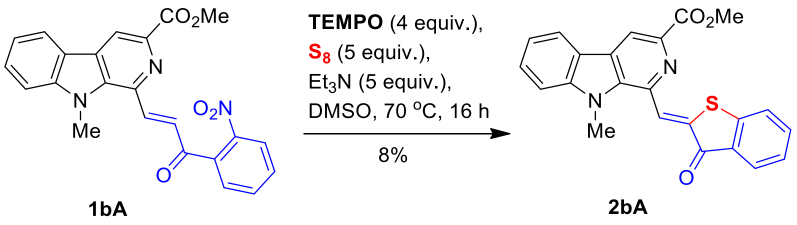
Inspired by the results of the above study, it was envisaged to check the generality of this strategy for the synthesis of β-carboline linked benzothiophene derivative. Accordingly, we employed 1-acetyl-β-carboline [24] (**5**) for Claisen-Schimdt condensation with 2-nitrobenzaldehyde (**C**) in the presence of Cs_2CO_3 and anhydrous THF at room temperature. The product **5C** was obtained as a major product along with some unidentified impurities. The evaporation of excess solvent (THF) followed by the treatment of resultant crude 2-nitrochalcone **5C** with Et_3N and elemental sulphur in DMSO at 70 °C furnished the expected product **6C**, albeit in low yield (39%) as shown in Scheme 6. It is important to mention that Claisen-Schmidt



Scheme 6. One-pot synthesis of β-carboline linked benzothiophene derivative.

condensation of **5** with 2-nitrobenzaldehyde (**C**) could not be achieved with KOH in MeOH or Cs_2CO_3 in DMSO.

To probe the reaction mechanism, a control experiment was conducted with model substrate **1bA** in presence of a radical-scavenger (TEMPO) to check the possibility of a radical mechanism vs electrophilic addition of sulphur [20e] (Scheme 7). It was observed that the reaction could not be completed even after 24 h in presence of TEMPO; though, earlier it required only 20 min for completion under standard conditions. Thus, the reaction followed the radical pathway and an electrophilic addition of sulphur was ruled out.



Scheme 7: Control experiment.

Based on our observations during the present study and previous reports [20e], a plausible mechanism for the formation of benzothiophenone ring is depicted in Figure 2. It is anticipated that initially formation of trisulfur radical anion ($S_3^{\cdot -}$) occurs *via* reaction of elemental sulphur with triethylamine in DMSO. The addition of trisulfur radical anion to the alkene in 2-nitrochalcone (**1bA**) may yield the intermediate **7**. Further abstraction of hydrogen in intermediate **7** may result in formation of intermediate **8**. The cleavage of S-S bond in **8** under basic conditions may generate sulphur anion **9**. The nucleophilic substitution reaction by transit sulphur anion in **9** followed by dismissal of nitrite ion may result in formation of β-carboline tethered benzothiophenone derivative **2bA**. It is anticipated that the role of DMSO is to stabilize the ionic intermediates; specifically **10** and to speed-up the transformation.

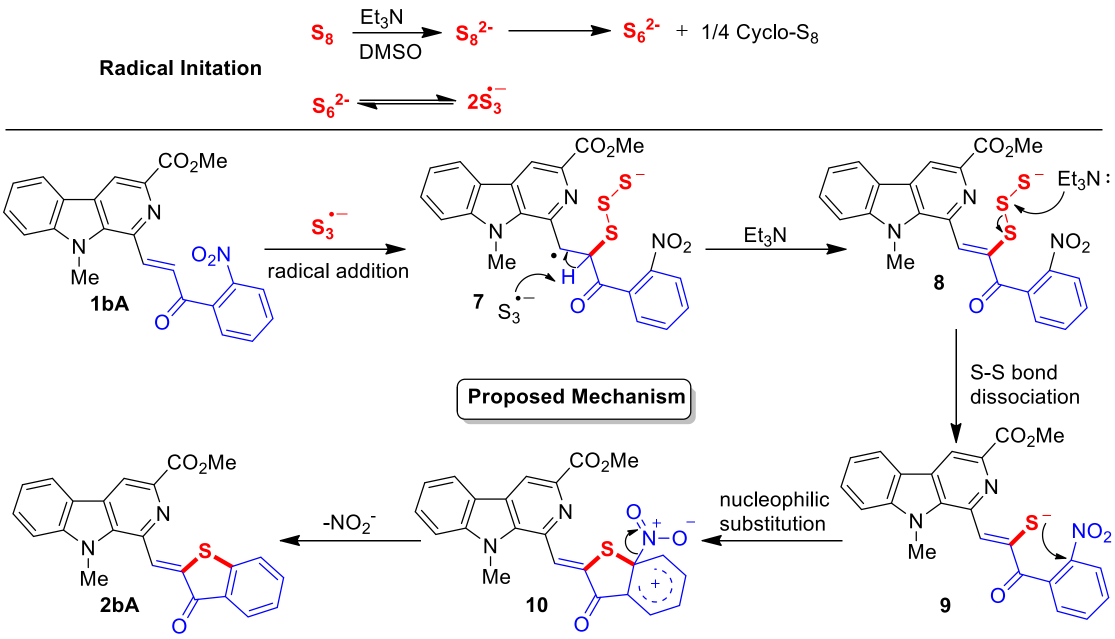


Figure 2. Proposed reaction mechanism.

Photophysical Studies

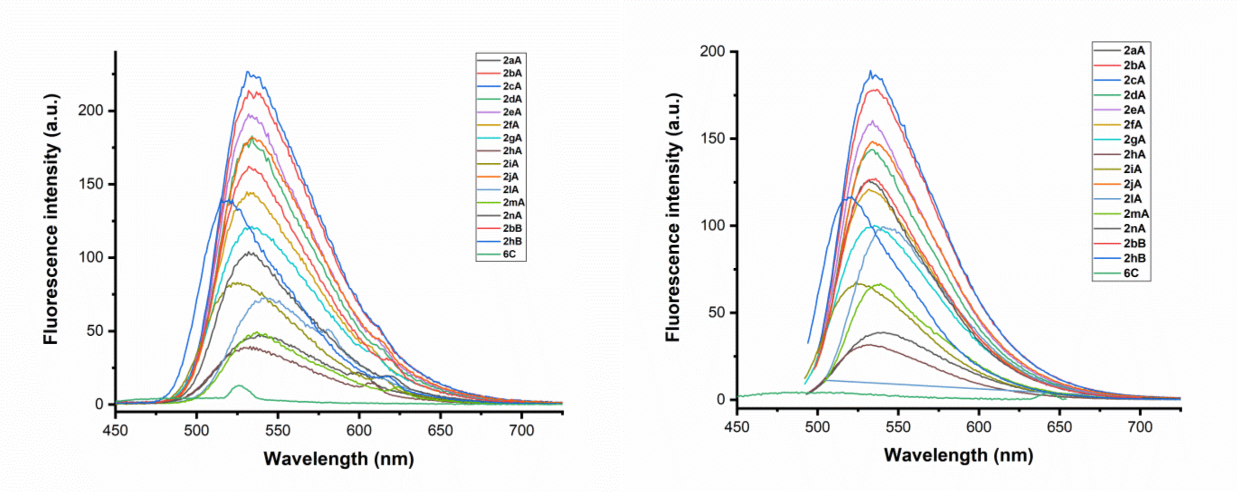
Fluorescence being a non-destructive exceptional technique to monitor a system of interest at a molecular level [25], this technology has found wide-ranging applications in several research areas such as medicine, pharmaceutics, biology, environment and food science [26]. Therefore, the light emitting properties of novel β-carboline C-1 as well as C-3 substituted benzothiophenone derivatives (**2aA-nA**, **2bB**, **2hB**, **4aA-gA**, **4eB** and **6C**) were evaluated to stimulate their further exploration for application in the field of material science as chemosensors, ligands and fluorescent probes. In order to investigate the fluorescence properties, compound **2bA** was chosen as the model substrate for optimization of various parameters like time, concentration and solvent. To obtain the maximum emission, various solvents were screened. The synthesised compounds showed best solubility and displayed maximum intensity in $CHCl_3$ as compared to other solvents (DMSO, DMF and MeOH). No considerable change in the fluorescence intensity of fluorophores was observed even after 5 h of sample preparation. Next, after careful analysis of concentrations, 4 µM concentration in $CHCl_3$ was found to be optimal for photophysical studies of the synthesized derivatives.

Having a series of diversely substituted β-carboline C-1 or C-3 tethered benzothiophenone derivatives, we carefully measured their photophysical properties including absorptions, excitations, emissions and fluorescence quantum yields in $CHCl_3$. The photophysical data of all the compounds are summarised in Table 2 and their graphical data is depicted in Figures 3-6. The fluorescence quantum yield (Φ_F) was measured relative to quinine sulphate (Φ_R = 0.546 in 0.1 M H_2SO_4 under 350 nm excitation) as a reference compound. For the measurement of UV-Vis absorption and fluorescence emission of samples, stock solutions of 1.0 mM concentration were prepared and diluted to 4.0 µM concentration using $CHCl_3$ as the solvent. The quantum yields were calculated as per this equation:

$$\Phi_S = \Phi_R \times \frac{I_S}{I_R} \times \frac{A_R}{A_S} \times \frac{{\eta_S}^2}{{\eta_R}^2}$$
$$R - \text{Reference}\,;\, S - \text{Sample}$$

Due to spin-orbit coupling, thiophene-based fluorophores generally show weak fluorescence emission which may be attributed to the heavy atom effect of the sulphur mediated by charge transfer mixing. It is worth mentioning that the majority of β-carboline substituted benzothiophenone derivatives showed strong fluorescence. The emission maxima of these fluorophores showed a wide region of fluorescent emissions (λ_{Em}, 490–582 nm in $CHCl_3$) along with large Stokes shifts (up to 293 nm), excellent quantum yields (up to 47%) and high brightness (up to 11196). The brightness of fluorophores was calculated by the multiplication of quantum yield (Φ) with its molar extinction coefficient (ε).

In case of β-carboline C-1 substituted benzothiophenones (**2aA-nA**, **2bB** and **2hB**), the substituents at R^1 and R^2 significantly affected the fluorescence of the compounds. It was noted that the fluorescence increased with lengthening of alkyl chain at N-9 (R^2) and followed the order as *n*-Bu > *n*-Pr > Et > Me > H. The β-carboline derivative with free N-H (N-9), **2aA** showed low fluorescence quantum yield (Φ_F = 18%) in this series (Table 2 and Figures 3). The presence of benzyl group at R^2 **(2hA)** improved the photophysical properties including high quantum yield (Φ_F = 47%). With variation in substituents at R^1 position, a regular pattern of fluorescence was observed *i.e.* CO_2*i*-Pr > CO_2Me > H which may be attributed to the electron-withdrawing nature of substituents (ester group) at C-3 of β-carboline ring.



(a) excited (λ_{Ex}) at 269-311 nm

(b) excited (λ_{Ex}) at 320-491 nm

Figure 3. Fluorescence spectra of **2aA-nA**, **2bB**, **2hB** and **6C**.

Table 2: Photophysical data of β-carboline tethered benzothiophenone derivatives

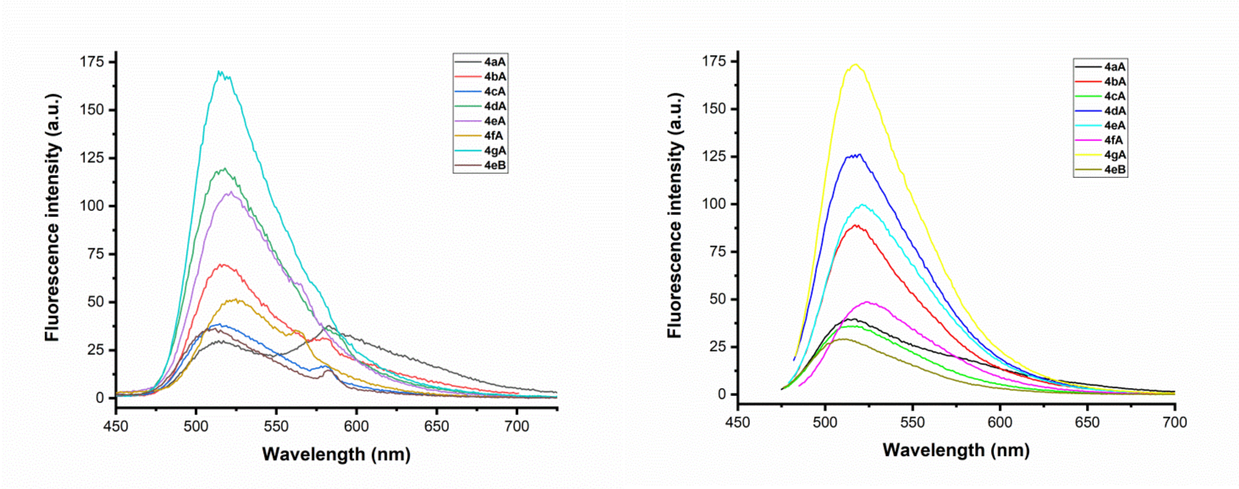
Compd.	UV-Vis[a]	Fluorescence			Stoke Shift	Molar Extinction Coefficient (ε)	Brightness
	λ_{Ex} (nm)	λ_{Em} (nm)	Intensity	Quantum Yield (Φ_F)[b]			
2aA	300.50	539.95	47.61	0.186	239.45	13750	2557
	481.00	540.88	38.78	0.295	59.88	6750	1991
2bA	305.20	531.94	213.81	0.229	226.74	45750	10477
	487.78	536.86	178.31	0.342	49.08	25000	8550
2cA	305.40	533.89	233.89	0.265	234.49	42250	11196
	488.18	532.83	193.36	0.347	44.65	26250	9109
2dA	306.13	534.02	182.87	0.274	227.72	31000	8494
	487.50	534.02	143.78	0.383	47.42	17250	6607
2eA	304.93	531.94	197.94	0.279	227.01	33250	9277
	487.49	534.02	160.50	0.400	46.53	18250	7300
2fA	303.41	530.89	144.88	0.256	227.48	27750	7104
	483.69	531.94	121.01	0.374	48.25	15500	5797
2gA	303.61	534.02	121.25	0.221	230.41	28500	6298
	480.49	535.07	100.11	0.328	54.58	15500	5084
2hA	303.21	532.98	39.57	0.302	229.77	6750	2038
	482.90	532.83	31.74	0.473	49.93	3250	1537
2iA	306.21	525.07	83.13	0.243	218.86	17000	4131
	480.08	524.91	67.85	0.337	44.83	9500	3201
2jA	305.89	534.02	181.82	0.304	228.13	29250	8892
	487.51	534.98	148.43	0.378	47.47	18750	7087
2lA	289.98	542.05	72.89	0.189	252.07	19500	3685
	492.53	541.08	99.43	0.253	48.55	18500	4680
2mA	311.59	537.01	49.49	0.223	225.42	10250	2286
	491.81	538.95	66.73	0.366	47.14	8000	2928
2nA	309.56	531.94	104.13	0.213	222.38	22750	4846
	487.74	531.79	126.29	0.349	44.05	16250	5671
2bB	309.67	531.94	162.21	0.301	222.27	25500	7675
	486.62	535.97	127.26	0.378	49.35	15500	5859
2hB	308.54	515.78	140.57	0.330	207.24	18750	6187
	482.71	521.54	116.95	0.258	38.83	8000	2064
4aA	289.82	522.94	37.76	0.052	293.12	60750	3159
	463.50	512.83	39.76	0.095	49.33	24250	2304

4bA	289.62	514.64	69.79	0.167	225.02	22500	3757
	380.09	518.04	40.58	0.179	137.95	10750	1924
	470.77	517.02	89.14	0.219	46.25	17750	3887
4cA	289.17	514.91	38.82	0.079	225.74	25000	1975
	465.41	518.05	36.06	0.179	52.64	9250	1656
4dA	293.41	518.05	119.83	0.160	224.64	35750	5720
	470.59	520.01	126.18	0.291	49.42	19500	5674
4eA	282.56	521.94	107.64	0.111	239.38	46750	5189
	376.41	519.85	63.43	0.141	143.44	23500	3313
	466.89	521.04	99.98	0.196	54.15	23250	4557
4fA	280.74	524.92	51.79	0.080	244.18	32500	2600
	383.74	520.89	29.12	0.141	137.15	11750	1657
	473.79	522.98	48.80	0.158	49.19	13750	2172
4gA	288.53	514.02	170.41	0.252	225.49	29500	7437
	380.11	517.01	86.20	0.284	136.90	13000	3692
	471.56	517.90	173.56	0.257	46.34	21500	5525
4eB	291.19	511.94	36.39	0.150	220.75	12250	1837
	464.27	508.04	29.47	0.225	43.77	4250	956
6C	263.14	525.96	13.60	0.034	262.82	15000	510
	320.64	490.41	4.48	0.016	169.77	18750	300

[a]Measured at 4 µM concentration in $CHCl_3$; [b]Quantum yields (Φ_F) were determined with reference to quinine sulfate.

Interestingly, a similar trend was observed in β-carboline C-3 substituted benzothiophenone derivatives (**4aA**-**gA** and **4eB**). Compared to **4aA** and **4aC** bearing aliphatic substituents at C-1 (R^4), compound **4eA** with aromatic substituent exhibited better fluorescence due to extended conjugation. The effect of R^2 substituent in these derivatives (**4bA**, **4dA**, **4fA** and **4gA**) was also investigated and it was found that *N*-alkylation improved the photophysical properties along with higher quantum yields (Figure 4). With regard to the impact of R^3 substituent, thiopheneone derivatives with chloro substitution (**2bB** and **4eB**) displayed higher quantum yield than unsubstituted derivatives

(**2bA** and **4eA**) as evident from Table 2. Overall, it can be concluded that β-carboline C-1 substituted benzothiophenone derivatives exhibited better photophysical properties including high quantum yield, brightness and significant bathochromic shift in the emission wavelengths. In short, β-carboline substituted benzothiophenone derivatives emerged as excellent fluorophores and displayed excellent photophysical properties with quantum yield (Φ_F) up to 47%. It is believed that these compounds may find applications in material science and biomedical investigations.



(a) excited (λ_{Ex}) at 280-293 nm **(b)** excited (λ_{Ex}) at 463-473 nm

Figure 4. Fluorescence spectra of **4aA-gA** and **4eB**.

Conclusion

In summary, an efficient synthesis of highly fluorescent β-carboline linked benzothiophenone derivatives have been successfully accomplished through one-pot metal free approach for the first time. The transformation could be executed from β-carboline-based 2-nitrochalcones *via* one-pot, two-step procedure starting from 1(3)-formyl β-carbolines (a framework represented by alkaloid Kumujian C). The combination of Et_3N and DMSO played a vital role in activation of sulphur resulted in the formation of two C-S bonds in single operation. This strategy offers several advantages, such as one-pot procedure, operational simplicity, easy purification, use of inexpensive reagents and wide functional group compatibility. Importantly, the presence of two important pharmacophores along with exocyclic double bond with Michael acceptor properties in the title compounds offers the opportunity to explore their biological potential. Moreover, these β-carboline linked benzothiophenones displayed excellent fluorescence properties with quantum yield (Φ_F) up to 47%. The detailed studies are underway in our laboratory to understand the basics of these fluorophores and to synthesise novel fluorophores with improved photophysical properties which can easily find application in material science.

Experimental Section

General experimental procedure for the synthesis of β-carboline based 2-nitrochalcone derivatives (1aA, 1bA, 1dA and 1hA) as exemplified for compound 1bA. To a stirred solution of KOH (0.033 g, 0.587 mmol) in dry MeOH (4 mL), 2-nitroacetopehnone (**A**, 0.080 mL, 0.587 mmol) was added at room temperature and the reaction mixture was stirred for 15 min. Thereafter, **1b** (0.15 g, 0.560 mmol) was added portion-wise and the reaction mixture was allowed to stir for additional 1 h at room temperature. After completion of reaction (as monitored by TLC), the precipitates were filtered through sintered funnel, washed twice with anhydrous MeOH and dried under vacuum to obtain the analytically pure product **1bA**, 0.20 g (86%) as a yellow solid.

General experimental procedure for the synthesis of β-carboline C-1 substituted benzothiophenone derivatives (2aA, 2bA, 2dA and 2hA) as

exemplified for compound 2bA. A 10 mL round bottom flask was charged with nitrochalcone **1bA** (0.20 g, 0.482 mmol), Et_3N (0.336 mL, 2.41 mmol), sulphur powder (0.077 g, 2.41 mmol), DMSO (1 mL) and the reaction mixture was stirred at 70 ^oC for 20 min. After the completion of reaction, as analysed by TLC, the crude product was directly purified by silica gel column chromatography (eluent; $CHCl_3$/MeOH, 95:5, v/v) without aqueous treatment to afford 0.15 g of **2bA** (78%) as orange solid.

One-pot experimental procedure for the synthesis of β-carboline C-1(3) substituted benzothiophenone derivatives (2aA-nA, 2bB, 2hB, 4aA-gA and 4eB) as exemplified for compound 2bA. To a stirred solution of KOH (0.033 g, 0.587 mmol) in dry MeOH (4 mL) in a 10 mL round bottom flask; 2-nitroacetopehnone (0.080 mL, 0.587 mmol) was added at room temperature and the reaction mixture was stirred for 15 min. Thereafter, methyl 1-formyl-9-methyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (**1b**) (0.15 g, 0.560 mmol) was added portion-wise and the reaction mixture was allowed to stir for additional 1 h at room temperature. After completion of reaction (as detected by TLC), the reaction content was allowed to settle for 5 min and MeOH was decanted and evaporated under reduced pressure. Thereafter, DMSO (1.5 mL) was added to the crude product **1bA** (nitrochalcone) followed by sequential addition of sulphur powder (0.089 g, 2.80 mmol) and Et_3N (0.390 mL, 2.80 mmol) at room temperature. The reaction mixture was stirred at 70 ^oC for 20 min. After the completion of reaction (as analysed by TLC), the product **2bA** was directly purified through column chromatography on silica gel using $CHCl_3$/MeOH, (95:5, v/v) as an eluent to afford the analytically pure product **2bA** as orange solid in 74% yield (two step yield).

One-pot experimental procedure for the synthesis of methyl 1-(benzo[*b*]thiophene-2-carbonyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (6C). To a stirred suspension of Cs_2CO_3 (0.182 g, 0.560 mmol) in dry THF (4 mL) in a 10 mL round bottom flask, methyl 1-acetyl-9-benzyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (**5**; 0.10 g, 0.373 mmol) was added and stirred the reaction content for 10 min. Thereafter, 2-nitrobenzaldehyde (**C**, 0.062 g, 0.410 mmol) was added and the reaction mixture was stirred for additional 2 h at room temperature. After completion of reaction as revealed by TLC, THF was evaporated under reduced pressure. Next, the crude nitrochalcone **5C** was re-dissolved in DMSO (1 mL) followed by the addition of sulphur powder (0.060 g, 1.86 mmol) and Et_3N (0.260 mL, 1.86 mmol) at room temperature. The reaction mixture was stirred at 70 ^{o}C for 1 h. After the completion of reaction, the product was directly purified through silica gel column chromatography (eluent; hexane/EtOAc, 60:40, v/v) to afford 0.056 g (39%) of **6C** as a light brown solid (two step yield).

Supporting Information

Supporting Information File 1

General information, experimental procedures, spectroscopic data, photophysical data and copies of ^{1}H-NMR, ^{13}C-NMR and HRMS spectra.

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