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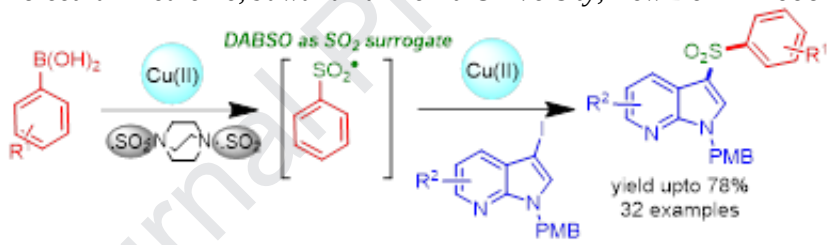

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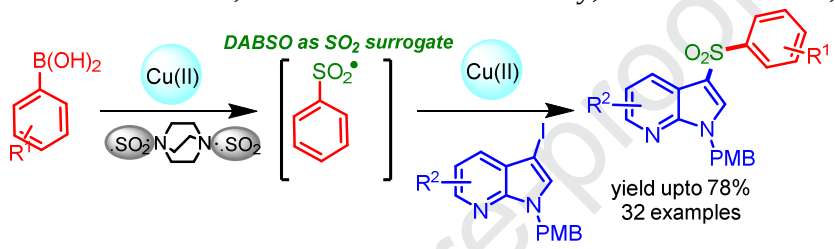

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ABSTRACT

DABSO mediated sulfonylation of iodinated 7-azaindoles was achieved for the first time through sulfonylative Suzuki-Miyaura cross coupling (SMC) reaction under mild conditions giving good yields of sulfonylated 7-azaindole derivatives. Interestingly, control experiments suggest that present method involves *in-situ* generation of $ArSO_2$ free radical followed by the key steps of SMC reaction. Scope of the reaction was explored with both electronically different and bulky group carrying boronic acids as coupling partner. The sulfonylation is scalable and occurred selectively at iodo group, irrespective of its position on azaindole. Moreover, the proposed mechanism has been supported by electron paramagnetic resonance (EPR) and density functional theory (DFT) calculations.

1. Introduction

7-Azaindole, a bioisosteric replacement of indole is found to be a prominent and pivotal target for the synthetic community, realizing its potency in plethora of medically beneficial activities.[1] Two drugs named Vemurafenib and Venetoclax, containing a 7-azaindole core are approved by FDA and several other 7-azaindole-containing species are in various stages of clinical development [2] (Fig.1A). One report on 1-aminoethyl-3-arylsulfonyl-1*H*-pyrrolo[2,3-*b*]pyridines as potent 5-HT_6 agonists shows the importance of sulfonyl azaindole compounds.[2g] Due to their medicinal/material properties, methods for the synthesis and functionalization of azaindole and its derivatives have attracted considerable interest.[3] The development of transition-metal-catalyzed reactions for the functionalization of heterocycles continues to be an active area of research.[4] In particular, C-sulfonylation is a favored organic transformation for the prospective enhanced biological features in heteroarenes.[5]

In recent years, DABSO has become a reagent of choice for the sulfonylation reactions as compared to other SO_2-surrogates due to its bench stability, commercial availability and easy handling.[6] Initially, Willis et al.[7a-b] and Rocke et al.[8] recommended DABSO for the *in-situ* formation of sulfinates

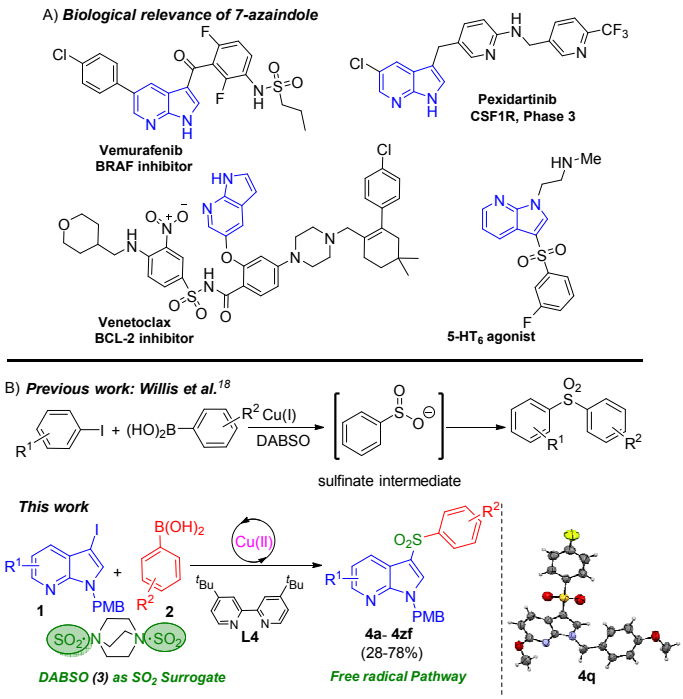
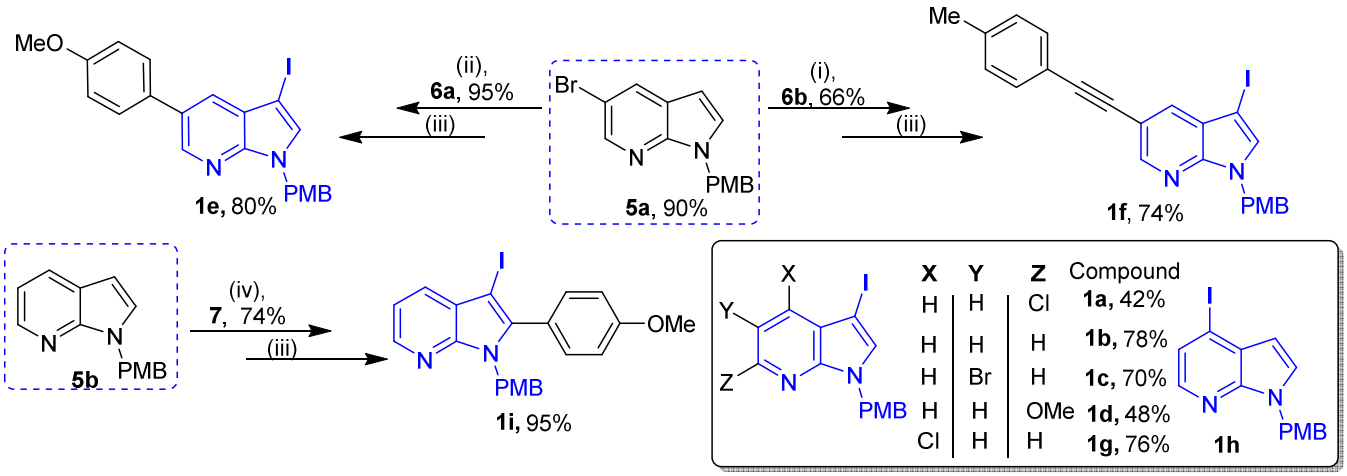


Fig. 1. [A] Biological relevance of azaindole [B] sulfonylative Suzuki-Miyaura cross coupling.



Scheme 1. Preparation of iodo-substituted 7-azaindoles (**1a-1i**). Reaction conditions: (i) under Ar atm., alkyne (1.2 equiv.), CuI (5 mol %), $PdCl_2(PPh_3)_2$ (5 mol %), NEt_3 (1.3 equiv.), DMF, 120 °C, 6-8 h; (ii) Ar-$B(OH)_2$ (1.2 equiv.), $Pd(OAc)_2$ (5 mol %), dppf (5 mol %), Cs_2CO_3 (2 equiv), 1,4-dioxane, 90° C, 1 h; (iii) NIS (1 equiv.), KOH (0.5 equiv.), DCM, 1 h, r.t.; (iv) iodoanisole (1.1 equiv), AgOTf (1.2 equiv.), dry DMF, $Pd(OAc)_2$ (10 mol%), *o*-nitrobenzoic acid (1.5 equiv.), 120° C, 3 h.

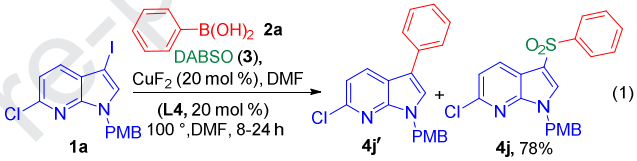
to fabricate sulfonamides afterwards sulfone synthetic protocols from organolithium/ magnesium[9] and organozinc reagent[10] were outlined. Synthesis of diverse range of important frameworks can be accomplished *via* sulfonylative alkyne chemistry,[11] reductive fluoroalkyl sulfination,[12] regio- and stereospecific selenosulfonation,[13] C(sp^2)–H arylsulfonylation[14] and oxidant or metal free strategy[15] concomitant with DABSO.[16] Notably, palladium and copper catalyzed direct C-H functionalization of indoles[17a] and imidazopyridines[17b] through SO_2 fixation was disclosed by certain groups. There are already reports on Cu(I)-catalyzed sulfonylative Suzuki–Miyaura cross-coupling between boronic acids, DABSO, and aryl iodides[18] (Fig.1B). Although coupling on substrate such as indole, pyrrole and quinolones is in the list, but they have not show it on pyridine fused rings, but overall yield of sulfonylated product on pyridine was 39% only. Based on the considerations above, this is first report of DABSO mediated sulfonylative SMC on hetrocyclic azaindole through free radicals. In continuation of our earlier work on Suzuki-Miyaura coupling studies on heteroaromatics,[19] a convenient copper (II) activated sulfonylative Suzuki-Miyaura coupling of azaindoles employing DABSO is being reported in this manuscript (Fig. 1B). The EPR and DFT calculations suggest that reaction is going through a free radical pathway.

2. Results and discussion

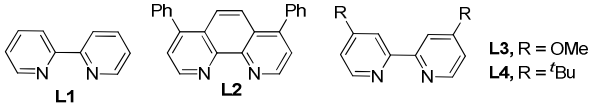
Preparation of Iodo-7-azindoles: A variety of iodo-7-azaindole (**1a-1i**) were synthesized from commercially available 7-azaindole to access the product. Literature method of iodination,[3d, 19a] *N*-oxidation,[19b] chlorination[19a] and *N*-protection[19a] were employed to gain iodo-7-azaindole as starting material in good to excellent yields. C-5 Br group was utilized to prepare **1e** and **1f** readily through Suzuki-Miyaura and Sonogashira cross-coupling reactions, while **1h** is synthesized by Finkelstein reaction[20f] for exchange of Cl-I group. Compound **1i** is prepared from C-H activation procedure given by Larossa et al.[20a]

The investigations began by establishing suitable reaction conditions for the coupling between 6-chloro-3-iodo-1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-*b*]pyridine (**1a**) and phenyl boronic acid (**2a**) in the presence of DABSO (**3**) (Table 1) leading to desired product **4j**. The dihalogenated azaindole was chosen in order to monitor selectivity of reaction.

Table 1. Optimization reactions for the synthesis of **4j** by coupling of **1a** and boronic acid **2a.**



Entry	Cu-catalyst	L	Solvent	4j´ (%)	4j (%)
1	$Cu(MeCN)_4BF_4$	**L1**	DMF	18	49
2[c]	$Cu(MeCN)_4BF_4$	**L1**	DMF	15	58
3	$Cu(MeCN)_4PF_6$	**L1**	DMF	45	31
4[d]	Cu_2O	**L1**	DMF	25	39
5[e]	CuBr	**L1**	DMF	38	34
6	$Cu(acac)_2$	**L1**	DMF	41	55
7	$Cu(OTf)_2$	**L1**	DMF	n.r.	n.r.
8	$Cu(NO_3)_2.3H_2O$	**L1**	DMF	58	40
9[f]	$Cu(acac)_2$	**L1**	DMF	36	24
10	CuF_2	**L1**	DMF	32	68
11	CuF_2	**L1**	DMF	21	78
12	CuF_2	**L2**	DMF	25	60
13	CuF_2	**L3**	DMF	21	71
14	CuF_2	**L4**	DMF	--	**78**
15	CuF_2	**L4**	ACN	--	58
16	CuF_2	**L4**	DMPU	22	66
17[g]	CuF_2	**L4**	DMF	n.r	n.r.
18[h]	CuF_2	**L4**	DMF	--	56
19[i]	CuF_2	**L4**	DMF	45	42
20	--	**L4**	DMF	n.r.	n.r.

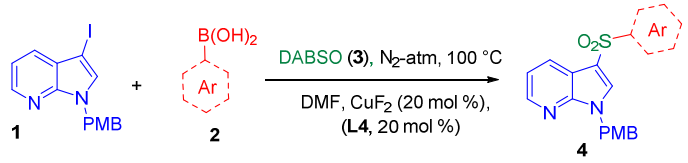


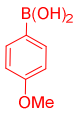
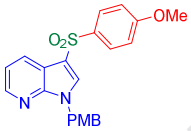
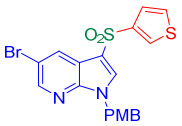
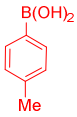
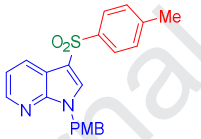
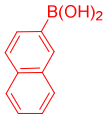
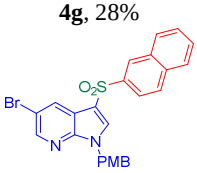
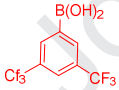
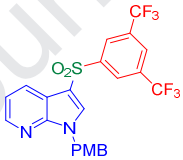
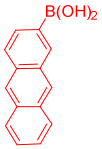
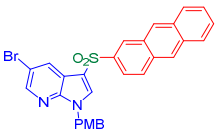
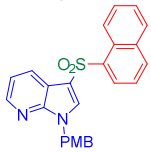
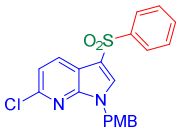
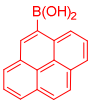
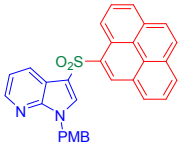
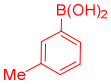
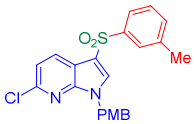
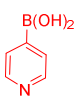
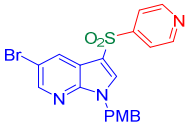
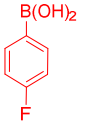
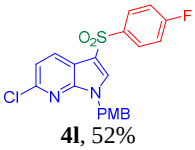
Reaction conditions: **1a** (80 mg, 0.2 mmol, 1.0 equiv.), DABSO (72 mg, 0.3 mmol, 1.5 equiv.), **2a** (29 mg, 0.24 mmol, 1.2 equiv.), CuF_2 (20 mol %), **L4** (20 mol %), dry DMF (0.067 M, 3-5 mL), N_2 atm., [b]Isolated Yields, [c]PG = Me, [d]15 % starting recovered, [e]12% starting recovered, [f]25% starting recovered, [g]reaction at rt, [h]reaction at 80°C and 35 % starting recovered, [i]reaction at 130° C, n. r. = No reaction.

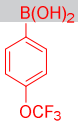
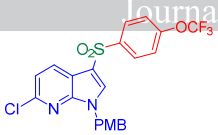
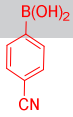
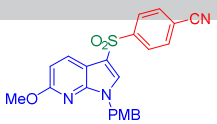
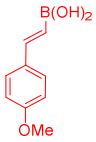
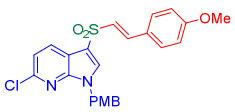
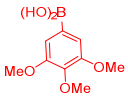
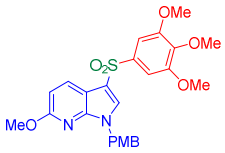
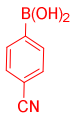
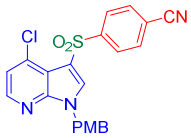
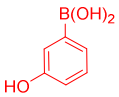
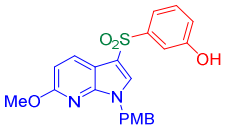
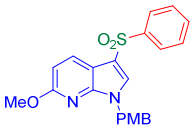
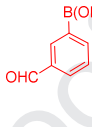
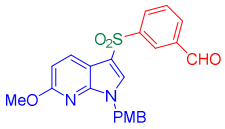
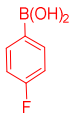
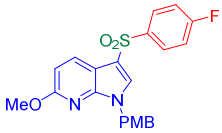
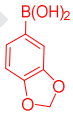
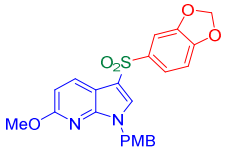
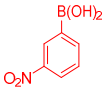
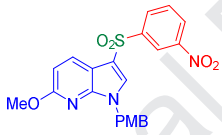
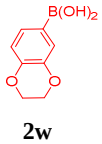
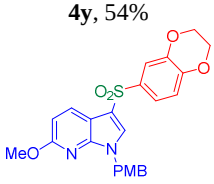
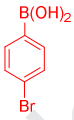
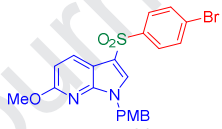
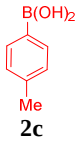
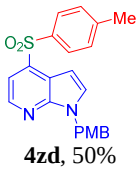
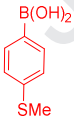
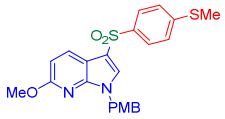
Initially we have pursued Willis strategy of $Cu(MeCN)_4BF_4$ catalyst with bipyridyl ligand (**L1**) in DMF at 100°C, which gave **4j** in 49% of yield with 18% of non-sulfonylated C-C coupling product **4j´**(Table 1, entry 1). We have used *N*-methyl protected azaindole but no improvement in the yield of **4j** was observed. When we changed the counter anion $(PF_6)^-$ 31% of sulfonylated product was obtained. However, inferior results were obtained with other copper salts *e.g.* Cu_2O, CuBr, $Cu(acac)_2$ (entries 4-6), while $Cu(OTf)_2$ failed to produce any desired product. (entry 7). Pleasingly, an increased yield of 68% was obtained with CuF_2 (entry 10). Use of nitrogen atmosphere promoted the yield to 78% but deterrent non-sulfonylative coupling product **4j´** remains a big hurdle (Table 1, entry 11). This reaction was also explored in other bipyridyl ligands, but almost similar results were obtained. Addition of 4,4′-di-tert-butyl-2,2′-dipyridyl as ligand in dried DMF and nitrogen atmosphere at 100°C, gave 78% **4j** exclusively (Table 1entry 14). Compound **4j** was isolated in low yield on solvent variation (Table 1, entries 17-18). Further, appropriate temperature was investigated as one of the requirement of sulfonylation reaction (Table 1, entry 17-19). Table 1, entry 20 suggests that catalyst is necessary for reaction. Therefore, optimized reaction conditions are as follows: **1a** (1equiv.), **2a** (1.2 equiv.), DABSO (1.5 equiv.), CuF_2 (20 mol %), **L4** (20 mol %), in dry DMF under nitrogen atmosphere at 100 °C (Table 1, entry 14).

To determine the viability of proposed method, sulfonylative coupling at C-3 position of 3-iodo 7-azaindoles (Table 2) was investigated first. Boronic acids having electron donating (EDG) and electron withdrawing groups (EWG) efficiently coupled with the unsubstituted C3-iodo 7-azaindoles to give **4a-4c** in 45-60%

Table 2. Scope of the sulfonylative Suzuki-Miyaura coupling for the substituted Iodo 7-azaindole[a,b]



Entry	(1a-d, 1g)	(2a-w)	4a-z (Yield)[a,b]	Entry	(1a-d, 1g)	(2a-w)	4a-z (Yield)[a,b]
1	**1b**	 **2b**	 **4a**, 54%	7	**1c**	 **2h**	 **4g**, 28%
2	**1b**	 **2c**	 **4b**, 60%	8	**1c**	 **2i**	 **4h**, 68%
3	**1b**	 **2d**	 **4c**, 45%	9	**1c**	 **2j**	 **4i**, 71%
4	**1b**	 **2e**	 **4d**, 64%	10	**1a**	 **2a**	 **4j**, 78%
5	**1b**	 **2f**	 **4e**, 35%	11	**1a**	 **2k**	 **4k**, 57%
6	**1c**	 **2g**	 **4f**, 54%[c]	12	**1a**	 **2l**	 **4l**, 52%

13	**1a**	 **2m**	 **4m**, 46%	21	**1d**	 **2o**	 **4u**, 59%
14	**1a**	 **2n**	 **4n**, 42%	22	**1d**	 **2s**	 **4v**, 64%
15	**1g**	 **2o**	 **4o**, 35%	23	**1d**	 **2t**	 **4w**, 53%
16	**1d**	**2a**	 **4p**, 45%	24	**1d**	 **2u**	 **4x**, 59%
17	**1d**	 **2l**	 **4q**, 67%	25	**1d**	 **2v**	 **4y**, 54%
18	**1d**	 **2p**	 **4r**, 54%	26	**1d**	 **2w**	 **4z**, 49%
19	**1d**	 **2q**	 **4s**, 51%	27	**1h**	 **2c**	 **4zd**, 50%
20	**1d**	 **2r**	 **4t**, 57%				

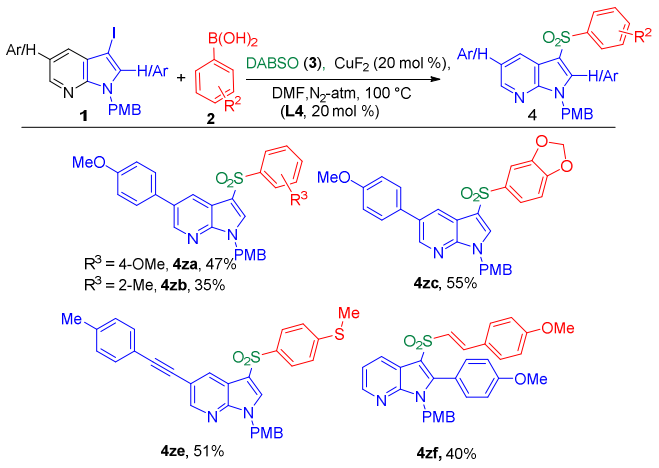
[a]Reaction conditions: **1a** (0.5 mmol, 1.0 equiv.), DABSO (0.75 mmol, 1.5 equiv), **2a** (0.6 mmol, 1.2 equiv.), CuF_2 (20 mol %), **L4** (20 mol %), dry DMF (3-5 mL), N_2-atm, 6-12 h, 100 °C, [b]Isolated yield. [c]15-18 h.

yield. The flat aromatic system **4d** & **4e** could be obtained in 64% and 35% yield respectively. Interestingly, C-5 Br-substituted 3-iodo-7-azaindoles too showed constructive sulfonylation where 4-pyridyl boronic acid smoothly proceeded to yield 54% of **4f**. Treatment of bulky 2-naphthyl and anthracene-2-boronic acid provided the desired products in good range of yield (68-71%, **4h**-**4i**). Compound 3-thienyl sulfonylated 7-azaindole **4g** was synthesized in 28% yield only. The sulfonylation of 6-chloro-7-azaindoles were explored to examine the effect of electronic variability on sulfonylation reaction. Remarkably, good yield of 1-(4-methoxybenzyl)-3-(phenylsulfonyl)-1*H*-pyrrolo[2,3-*b*] pyridine (78%, **4j**) was achieved. Installation of 3-Me, 4-F and 4-OCF_3 substituted phenyl boronic acid was carried out in 46–57% of yield (**4k**-**4m**) in the case of 6-chloro-7-azaindole.

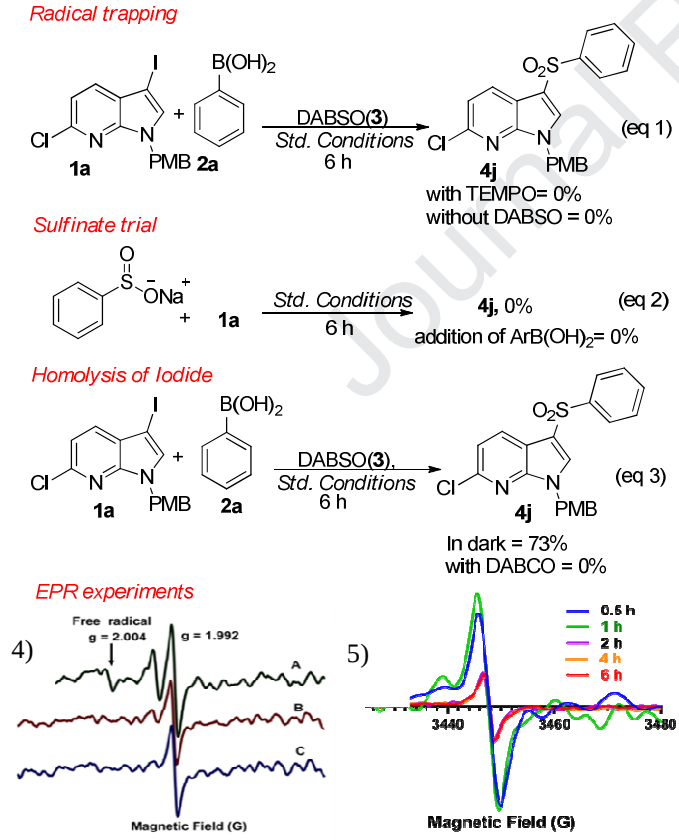
Vinyl boronic acid was also investigated as coupling partner to synthesize **4n** in 42% yield. Similarly, C-4 chloro substituted 3-iodo-7-azaindole also afforded C-3 sulfonylated product **4o** as a demonstration of synthetic elaboration of reaction

Further, sulfonylative coupling to C6-methoxylated-3-iodo azaindole was performed using electronically different aryl boronic acids in the three component reaction to get **4p**-**4z** in moderate to good yield. The reaction showed good tolerance towards functional groups such as -NO_2, -SMe, -CN, -OH, -CHO to get **4r**, **4t**-**4u**, **4w**-**4x** in good yield. Further, bicyclic heteroaryls containing boronic acids were reacted with 6-methoxy substituted 7-azaindoles to get **4y** (49 % yield) and **4z** (54% yield). Importantly, 4-iodo-7-azaindole prepared by Finkelstein reaction, furnished **4zd** in 50% yield.

This methodology is also useful in conjunction with C-C cross-coupling reactions such as Suzuki-Miyaura (**4za-4zc**) or Sonogashira coupling (**4ze**) for example; coupling of sterically hindered 2-methylphenyl boronic acid results 35% of **4zb**. C-2 arylated 7-azaindoles synthesized by C-H activation[20a] was also studied as substrate with trans-2- phenylvinyl boronic acid and **4zf** was isolated in moderate yield of 40% (Scheme 2).



Scheme 2. Sulfonylative Suzuki-Miyaura coupling, reaction conditions: **1a** (0.5 mmol, 1.0 equiv.), DABSO (0.75 mmol, 1.5 equiv.), **2a** (0.6 mmol, 1.2 equiv.), CuF_2 (20 mol %), **L4** (20 mol %), dry DMF (3-5 mL), N_2-atm, 6-12 h, 100 °C, Isolated yield.

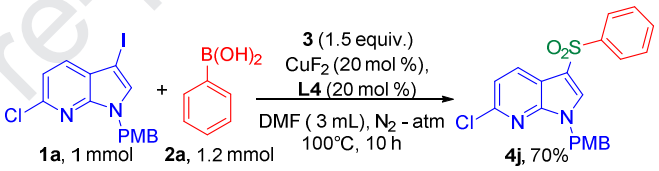


Scheme 3. Control Experiments. [4] EPR spectra of A) Reaction mixture (**1a** + **2a** + **3** + CuF_2+ **L4)** in DMF at 100°C at 10 mins, B) at 0 mins C) CuF_2+ **L4** in DMF at 0 mins. [5] Reaction mixture (**1a** + **2a** + **3** + CuF_2+ **L4**) in DMF at 100°C at different time points.

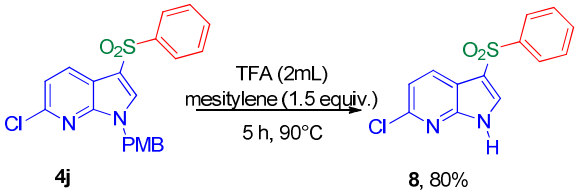
The structure of two compounds **4q** and **4x** was unambiguously confirmed through X-ray crystal structure analysis, which is given in supplementary information (Fig. S1 to S4).

To gain insights into the mechanism of the reaction, control experiments were performed (Scheme 3). Under standard conditions, the reaction was inhibited with TEMPO (eq 1). This observation suggests that the reaction is proceeding through a radical pathway which is different from the earlier report.[18]. The present methodology failed to produce the desired **4j** when readily prepared sulfinate was used as sulfonylation source (eq 2). The reaction did not work either in absence of DABSO or in presence of DABCO (eq 1 and 3), suggesting a different mechanism of sulfonylation as compared to sulfinate mediated sulfonylation.[18] The reaction underwent in dark (eq 3), which eliminates the possibility of light mediated homolysis of iodine.[21] This reaction is selective to iodo group on heterocyclic ring, irrespective of its position. Reaction did not go on chloro or bromo substituents. EPR proved the formation of delocalized free radical (g = 2.004) after 10 mins, except for paramagnetic Cu (II) (g = 1.992) (Scheme 3 (4)). Formation of Cu(I) in the reaction medium is evidenced by a decreased intensity of Cu(II) in time dependent EPR experiment [Scheme 3(5)].

The gram scale reaction using the standard conditions yielded 70% of the desired product **4j** (Scheme 4). The deprotection of *p*-methoxybenzyl group (PMB) is carried out on **4j** to yield free NH- group, using trifluoroacetic acid (TFA) (Scheme 5).[22]



Scheme 4. Large Scale Synthesis of **4j**



Scheme 5. Deprotection of PMB.

To explore the energy profile of the catalytic step of the reaction, quantum chemical calculations were performed using density function B3LYP method. The 3D structures of all the species and their absolute energy values are provided in supplementary information. The overall energy of the reaction requires about 27 kcal/mol (endergonic). However, the participation of the catalyst is facilitating the reaction (Fig. 2), by releasing ~36.1 kcal/mol energy. The energy profile of the reaction indicates the formation of an intermediate complex **C**, which is ~24 kcal/mol less stable than the starting species **1a**' and **B**.

Based on the aforementioned experimental observations and previous reports, a plausible mechanism was proposed (Scheme 6). Initially, Cu(II) gets reduced to Cu(I) in the presence of **L4** ligand to generate **A**.[23] Meanwhile, arylsulfonyl radical is produced by reaction of boronic acid and DABSO.[24] Afterwards, arylsulfonyl radical combines with the species **A** , forming Cu(I)-S bond (**B**) followed by oxidative addition of **1a**, which affords the intermediate **(D)**. Finally, the intermediate **(D)** undergoes

reductive elimination, leading to the desired product **4j**, and release CuI, followed by halogen exchange generate Cu(I)F.

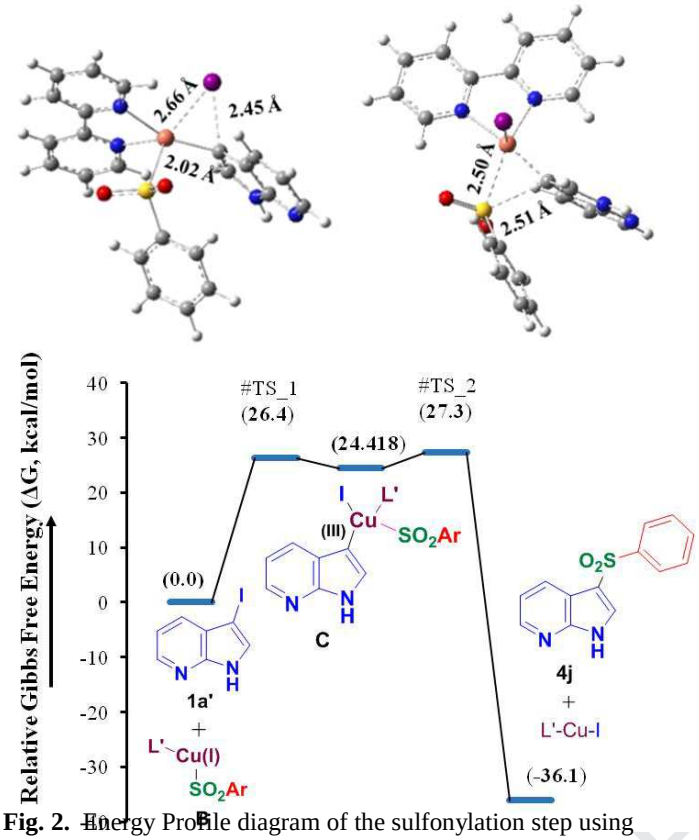
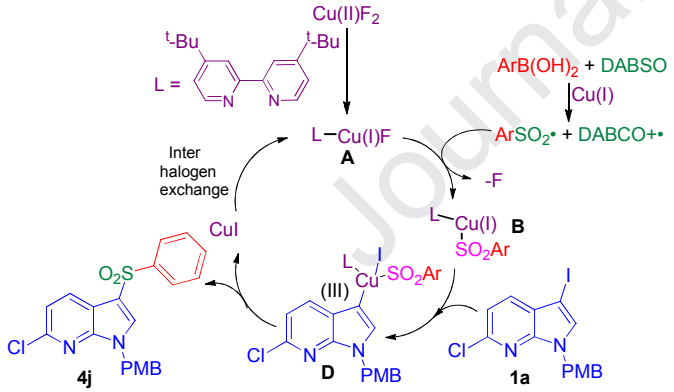


Fig. 2. Energy Profile diagram of the sulfonylation step using $B3LYP_3$ function with the 6-31+G(d) basis set for H, C, N, S and O atoms, and LAN2LDZ4 basis set for Cu and I. The two transition states are shown as TS1 and TS2.



Scheme 6. Plausible mechanism

3. Conclusions

In conclusion, successful incorporation of SO_2 to construct a C-S-C bond *via* copper catalyzed Suzuki-Miyaura sulfonylative coupling reaction has been attained. Here, *in situ* free radical formation followed by Suzuki-Miyaura coupling steps are the route to sulfones using DABSO as an SO_2 surrogate. Interestingly, no free radical initiators were used for this reaction. The proposed mechanism is supported by DFT calculation. Overall, we have developed an efficient method to synthesize medicinally important azaindolyl sulfones in good yields.

4. Experimental

4.1.1. General Information

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All Sulfonylative Suzuki-Miyaura reactions were performed in round bottom flask and monitored through thin layer chromatography (TLC silica gel F_{254}, glass plates) and analysed using 254 nm UV light and Iodine, ninhydrin stains. Melting points were recorded on Büchi Melting Point B-545 instrument and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded with a 400 MHz (^{1}H = 400 and ^{13}C = 100 MHz) or 500 MHz (^{1}H = 500 and ^{13}C = 125 MHz) spectrometer. Chemical shifts value of ^{1}H NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane (TMS, 0.00 ppm). Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), coupling constants (J) were reported in Hertz (Hz) and integration value. Chemical shifts value of ^{13}C NMR were recorded in parts per million (ppm, δ) and calibrated to the residual peak as an internal standard ($CDCl_3$: δ = 77.0 ppm and DMSO: δ= 39.0 ppm). High-resolution mass spectra (HRMS) were obtained using ESI-TOF method. EPR: Electron Paramagnetic Resonance spectra were recorded using Bruker EMX 1444 EPR spectrometer operating at 9.66 GHz. Diphenylpicrylhydrazyl, DPPH (g = 2.0037), was used for the calibration of EPR spectrometer. Infrared measurements were carried out as liquid films on NaCl discs or as a KBr disc using a Perkin-Elmer 1600 series FTIR spectrometer and Bruker Tensor 27 FT-IR with internal calibration in the range 4000- 500 cm^{-1}. MALDI-TOF MS measurements were performed with AB SCIEX TOF/TOF 5800 System with ekspert nanoLC 400 and EKSpot MALDI Spotter without using any matrix.

4.1.2. Reagents.

All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of dimethylformamide, acetonitrile, dimethyl sulfoxide, diethylether, THF, hexanes, ethyl acetate, and CH_2Cl_2 were purchased from Merck Chemical Co. 7-Azaindole, 5-bromo-7-Azaindole, *p*-methoxybenzylchloride, silver triflate,4-iodoanisole, $PdCl_2(PPh_3)_2$, dppf, terminal alkynes, palladium(II) acetate, Et_3N and the copper salts were purchased from Aldrich Chemical Co. Inc.

4.1.3. Preparation of starting Iodo-7-azindoles

A variety of iodo-7-azaindole (**1a-1i**) were synthesized by commercially available 7-azaindole to access the designed strategy. The **1a** was prepared from 1*H*-pyrrolo[2,3-*b*]pyridine with general procedure A, B, C and D, **1b** was synthesized from 1*H*-pyrrolo[2,3-*b*]pyridine with general procedure C and D, **1c** was synthesized starting from 5-bromo-1*H*-pyrrolo[2,3-*b*]pyridine with general procedure C and D, **1d** was syntheiszed from 1*H*-pyrrolo[2,3-*b*]pyridine with general procedure A, I, C, D, **1g** was synthesized from 4-chloro-1*H*-pyrrolo[2,3-*b*]pyridine with general procedure C and D. C-5 Br group was utilized to prepare **1e** and **1f** readily through cross-coupling reactions on 5-bromo-1*H*-pyrrolo[2,3-*b*]pyridine and 5-bromo-1*H*-pyrrolo[2,3-*b*]pyridine respectively. The **1h** was synthesized from 4-chloro-1*H*-pyrrolo[2,3-*b*]pyridine with general procedure H and D. Compound **1i** is synthesized from 1*H*-pyrrolo[2,3-*b*]pyridine with general procedure D, G and C. All general methods are written below for the ease of undersanding. The structure and purity of starting materials

and intermediates were confirmed by their physical and spectral data.

General method (A) for Iodination[3d,19a-b]

In a mixture of 1*H*-pyrrolo[2,3-*b*]pyridine (1 g, 1 equiv, 8.4 mmol) in CH_2Cl_2 was added KOH (235 mg, 4.2 mmol, 0.50 equiv.) at rt. After 30 min, *N*-iodosuccinimide (1.88 g, 8.4 mmol, 1.00 equiv) was added, and the mixture was stirred for 10 h, quenched with a saturated solution of $Na_2S_2O_3$, and extracted with CH_2Cl_2. The combined organic layers were dried and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc, 98:2) to give pure iodinated product. This method has been followed up for getting iodinated starting material (**1a**-**1i**).

General method (B) for N-oxide formation [19a-b] :

To a solution of 1*H*-pyrrolo[2,3-*b*]pyridine (1 g, 1 equiv, 8.4 mmol) in diethyl ether (50 mL) was added 77% m-chloroperbenzoic acid (21.1 mmol, 3.65 g, 2.5 equiv) portion wise. Then reaction mixture was stirred at rt for 1 h until a precipitation occurs. After the completion of reaction as monitored by TLC, it was filtered and dried. The obtained white solid added to 200 mL of distilled water, and saturated solution of potassium carbonate was slowly added to it, until pH of soultion reaches to 9−10. The mixture was stirred overnight, filtered, and dried to get an off-white solid. This method has been used in the preparation of **1a** and **1d** as written in above sequence.

General method (C) for Chlorination[19a-b] :

To a solution of 3-iodo-1*H*-pyrrolo[2,3-*b*]pyridine 7-oxide (1g, 3.8 mmol, 1 equiv) in dry THF, the N_2 was purged and an inert atmosphere was maintained. Added HMDS (620 mg, 3.8 mmol, 1 equiv), followed by slow addition of trichloroacetyl chloride (1.74 g, 9.6 mmol, 2.5 equiv) with constant stirring (ice bath). Then reaction mixture was stirred at room temperature for 1h and monitored using TLC. After completion, evaporated the THF and the mixture was extracted using EtOAc and washed with saturated solution of sodium bicarbonate. The organic layer was dried using anhydrous sodium sulfate and evaporated. Purification was done by using column chromatography on silica gel using ethyl acetate/hexane (30:70) to obtain a white solid. This method has been utilized for the preparation of **1a.**

General method (D) for N-protection[3a,19a-b]

To a solution of 3-iodo-1*H*-pyrrolo[2,3-*b*]pyridine (2 g, 8.2 mmol) in dry DMF (5 mL), added slowly K_2CO_3 (3.39 g, 3 equiv., 24.6 mmol) and stirred for 10 min. 4-Methoxybenzyl chloride (1.66 g, 1.3 equiv., 10.6 mmol) was added to solution and stirred the reaction mixture at rt. After the completion of reaction as indicated by TLC, the reaction was quenched with a sat. aq. NH_4Cl solution. The crude reaction mixture was extracted three times with CH_2Cl_2 and dried over anhyd. Na_2SO_4. After filtration, the solvent was removed *in vacuo*. Purification was done by column chromatography to furnish solid/oil. This method has been followed for getting **1a**-**1i** as mentioned above.

General method (E) for Suzuki-Miyaura reaction[19a]

A solution of 5-bromo-1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-*b*]pyridine **5a** (100 mg, 0.315 mmol), boronic acid (42.4 mg, 1.1 equiv., 0.34 mmol), $Pd(OAc)_2$ (3.5 mg, 0.05 equiv., 0.01 mmol), dppf (8.7 mg, 0.05 equiv., 0.01 mmol), Cs_2CO_3 (206.1 mg, 2 equiv., 0.63 mmol) in 1,4-dioxane : water (3:1, 3 mL) was heated to 90°C for 1 h. After the reaction was completed (monitored by TLC), the reaction was allowed to cool to room temperature. The reaction mixture was extracted with ethyl acetate and organic layer was washed with brine. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the desired product. This method has been followed up for getting **1e**.

General method (F) for Sonogashira reaction[19a]

A solution of 5-bromo-1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-*b*]pyridine **5a** (100 mg, 0.315 mmol), alkyne (38.7 mg, 1.2 equiv., 0.37 mmol), $PdCl_2(PPh_3)_2$ (11.1 mg, 0.05 equiv., 0.01 mmol), CuI (3.0 mg, 0.05 equiv., 0.01 mmol), NEt_3 (41.6 mg, 1.3 equiv., 0.41 mmol) in DMF (3 mL) was heated to 120 °C under N_2-atmosphere till reaction completed as indicated by TLC. The reaction was allowed to come to rt. The reaction mixture was extracted with ethyl acetate and organic layer was washed with brine. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the desired product. This method has been followed up for getting **1f** .

General method (G) for C-H activation[20a]

To the mixture of 1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-*b*]pyridine **5b** (100 mg, 0.41 mmol, 1.00 equiv.), iodoanisole (108 mg, 0.46 mmol, 1.1 equiv), AgOTf (129 mg, 0.5 mmol, 1.2 equiv.), dry DMF (10ml), added $Pd(OAc)_2$ (9.4 mg, 0.041 mmol, 10 mol%) and *o*-nitrobenzoic acid (105 mg, 0.62 mmol, 1.5 equiv.). The reaction mixture is allowed to stirred at 120° C for 3 h under N_2-atm. till completion of reaction as monitored by TLC. The reaction was allowed to cool to rt. The reaction mixture was extracted with ethyl acetate and organic layer was washed with brine. The combined organic layers were dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the desired product. This method is used for synthesis of **1i .**

General method (H) for Finkelstein reaction[20f]

To solution of 4-chloro-1*H*-pyrrolo[2,3-*b*]pyridine (1 g, 7.4 mmol), NaI (1.34 g, 1.2 equiv., 8.9 mmol), in MeCN (15 mL), AcCl (0.567 g, 1.1 equiv., 7.2 mmol) was refluxed under N_2 atm. till reaction completed as indicated by TLC (1.5h) stained with Iodine. The reaction was allowed to cool to room temperature. The reaction mixture was neutralized with 2M NaOH solution and solvent was evaporated, then it was taken in THF (10 ml) and stirred for next 12h at 40°C temperature. THF was evaporated and it was extracted with ethyl acetate and organic layer was washed with brine. The combined organic layers were dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the desired product. This method is followed up for the synthesis of **1h**.

General method (I) for methoxylation reaction[20f]

Under argon the 1*H*-pyrrolo[2,3-*b*]pyridine 7-oxide (3.0g, 22.39 mmol) was dissolved in dry MeCN (75 ml). Dimethylsulfate (2.37 ml, 24.62 mmol), was added and the reaction mixture was stirred at 65° C for 12 h. A CH_3ONa solution (3.08 g of sodium in 26 g of methanol) was added dropwise and the mixture was stirred for extra 20 h at 60° C. Then the reaction mixture was quenched with the acetic acid untill pH 7 was reached and concentrated. After dissolution it into DCM, the organic layer was washed with 1M sodium bicarbonate solution. The aqueous layer was combined and

extacted with ethyl acetate and dried over Na_2SO_4. The solvent was removed *in vacuo* and purification was done by silica gel column chromatography (hexane/EtOAc, 9:1) to furnished white solid. This method has been worked for synthesis of **1d**.

4.1.4. 6-Chloro-3-iodo-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridine ***(1a)***

Yield = 250 mg (88%); white color solid; mp = 87-88 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.59 (d, *J* = 8.2 Hz, 1H), 7.18 (d, *J* = 8.5 Hz, 2H), 7.15 (s, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 2H), 5.32 (s, 2H), 3.75 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.4, 146.1, 145.8, 131.9, 131.6, 129.5, 128.5, 121.7, 116.9, 114.2, 55.3, 54.0, 47.7. HRMS calcd. for $C_{15}H_{13}ClIN_2O(M+H^+)$: 398.9761. found: 398.9771.

4.1.5. 3-Iodo-6-methoxy-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridine ***(1d)***

Yield = 203 mg (72%); white color solid; mp = 80-81 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.58 (d, *J* = 8.5 Hz, 1H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.06 (s, 1H), 6.87 (d, *J* = 8.5Hz, 2H), 6.64 (d, *J* = 8.4 Hz, 1H), 5.32 (s, 2H), 4.03(s, 3H), 3.81 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 161.6, 159.2, 144.8, 131.9, 129.5, 129.3, 128.3, 116.9, 114.0, 104.9, 55.3, 53.8, 53.5, 47.5. HRMS calcd. for $C_{16}H_{16}IN_2O_2$ (M+H$^+$): 395.0256. found : 395.0280.

*4.1.6. 5-Bromo-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridine(****5a****)*

Yield = 228.6 mg (90%); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.39 (d, *J* = 2.0 Hz, 1H), 8.04 (d, *J* = 2.05 Hz, 1H), 7.20-7.18 (m, 3H, 1peak extra of $CDCl_3$), 6.86 (d, *J* = 8.6 Hz, 2H), 6.41 (d, *J* = 3.5 Hz, 1H), 5.40 (s, 2H), 3.79 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.2, 145.9, 143.4, 130.7, 129.3, 129.2, 129.0, 122.0, 114.1, 111.6, 99.5, 55.2, 47.5. HRMS calcd. for $C_{15}H_{14}BrN_2O(M+H^+)$: 317.0290. found : 317.0267.

*4.1.7. 1-(4-methoxybenzyl)-5-(4-methoxy phenyl)-1H-pyrrolo[2,3-b]pyridine(****6a****)*

Yield = 177.6 mg (95%); pale yellow solid; mp = 86-87 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.58 (d, *J* = 1.9 Hz, 1H), 8.08 (d, *J* = 2.0 Hz, 1H), 7.24-7.22 (m, 3H,), 7.05 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.54 (d, *J* = 3.4 Hz, 1H), 5.48 (s, 2H), 3.89 (s, 3H), 3.80 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.1, 158.9, 146.8, 142.1, 132.2, 129.8, 129.3, 128.9, 128.5, 128.4, 126.9, 120.6, 114.4, 114.1, 100.1, 55.3, 55.2, 47.4. HRMS calcd. for $C_{22}H_{21}N_2O_2$ (M+H$^+$): 345.1603. found: 345.1625.

4.1.8. 1-(4-methoxybenzyl)-5-(p-tolylethynyl)-1H-pyrrolo[2,3-b]pyridine ***(6b)***

Yield = 129 mg (66%); pale yellow color solid; mp = 120-121 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.53 (d, *J* = 1.7 Hz, 1H), 8.09 (d, *J* = 1.8 Hz, 1H), 7.48 (d, *J* =8.0 Hz, 2H), 7.21-7.18 (m, 5H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.47 (d, *J* = 3.5 Hz, 1H), 5.44 (s, 2H), 3.80 (s, 3H), 2.40 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.1, 146.5, 146.0, 138.2, 131.6, 131.4, 129.4, 129.1, 129.0, 128.7, 120.3, 119.9, 114.1, 112.1, 100.2, 89.7, 87.3, 55.2, 47.4, 21.5. HRMS calcd. for $C_{24}H_{21}N_2O$ (M+H$^+$): 353.1654. found : 353.1669.

4.1.9. 3-iodo-1-(4-methoxybenzyl)-5-(4-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridine ***(1e)***

Yield = 236.8 mg (74%); pale yellow color solid; mp = 155-156 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.57 (d, *J* = 2.0 Hz, 1H), 7.84 (d, *J* = 2.1 Hz, 1H), 7.61-7.59 (m, 2H), 7.29 (s, 1H), 7.24 (d, *J* = 8.6 Hz, 2H), 7.06-7.04 (m, 2H), 6.89-6.87 (m, 2H), 5.45 (s, 2H), 3.89 (s, 3H), 3.81 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.3, 159.1, 146.5, 143.3, 132.2, 131.6, 130.3, 129.2, 129.1, 128.5, 127.1, 123.0, 114.4, 114.2, 55.4, 55.3, 53.9, 47.7. HRMS calcd. for $C_{22}H_{20}IN_2O_2$ (M+H$^+$): 471.0569. found: 471.0573.

4.1.10. 3-Iodo-1-(4-methoxybenzyl)-5-(p-tolylethynyl)-1H-pyrrolo[2,3-b]pyridine ***(1f)***

Yield = 239.7 mg (74%); bright yellow solid; mp = 134-135 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.54 (s, 1H), 7.90 (s, 1H), 7.49 (d, *J* = 7.7 Hz, 2H), 7.24-7.20 (m, 5H), 6.88 (d, *J* = 8.2 Hz, 2H), 5.42 (s, 2H), 3.81 (s, 3H), 2.41(s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.4, 147.0, 146.2, 138.4, 132.6, 132.0, 131.4, 129.3, 129.2, 128.7, 122.6, 120.1, 114.2, 113.3, 90.5, 86.7, 55.3, 54.0, 47.7, 21.5. HRMS calcd. for $C_{24}H_{20}IN_2O(M+H^+)$: 479.0620. found : 479.0641.

4.1.11. 4-chloro-3-iodo-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridine ***(1g)***

Yield = 185 mg (65%); white color solid; mp = 107-108 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.23 (d, *J* = 5.1 Hz, 1H), 7.31 (s, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 7.11 (d, *J* = 5.1 Hz, 1H), 6.88-6.87 (m, 2H), 5.40 (s, 2H), 3.81 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 1C is less we observed. 159.4, 147.6, 143.6, 136.9, 133.9, 129.3, 128.5, 117.6, 114.2, 55.3, 49.0, 47.9. HRMS calcd. for $C_{15}H_{13}ClIN_2O(M+H^+)$: 398.9761. found : 398.9777.

4.1.12. 4-iodo-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridine ***(1h)***

Yield = 195 mg (72%); white color solid; mp = 71-72 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.99 (d, *J* = 5.0 Hz, 1H), 7.50 (d, *J* = 5.0 Hz, 1H), 7.24 (d, *J* = 3.4 Hz, 1H), 7.19 (d, *J* = 8.45 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.37 (d, *J* = 3.4 Hz, 1H), 5.41 (s, 2H), 3.79 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 1C is less we observed. 159.2, 145.6 142.8, 129.3, 129.0, 128.1, 125.2, 114.1, 103.1, 98.9, 55.2, 47.8. HRMS calcd. for $C_{15}H_{14}IN_2O(M+H^+)$: 365.0151. found : 365.0137.

4.1.13. 1-(4-methoxybenzyl)-2-(4-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridine ***(7)***

Yield = 184 mg (74%); white color solid; mp = 127-128 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.31 (dd, *J* = 5.9, 1.9 Hz, 1H), 7.89 (dd, *J* = 9.7, 2.0 Hz, 1H), 7.32-7.30 (m, 2H), 7.07 (dd, *J* = 9.7, 5.9 Hz, 1H), 6.92-6.89 (m, 4H), 6.73-6.71 (m, 2H), 6.47 (s, 1H), 5.47 (s, 2H), 3.83 (s, 3H), 3.72 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.7, 158.5, 149.1, 142.7, 141.7, 130.7, 130.6, 127.9, 127.8, 124.8, 120.7, 116.3, 113.9, 113.8, 99.6, 55.3, 55.2, 45.3. HRMS calcd. for $C_{22}H_{21}N_2O_2(M+H^+)$: 345.1603. found : 345.1603.

*4.1.14. 3-iodo-1-(4-methoxybenzyl)-2-(4-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridine(****1i****)*

Yield = 305 mg (95%); white color solid; mp = 142-143 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.39 (d, *J* = 4.6 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.28-7.27 (m, 2H), 7.20 (dd, *J* = 7.8, 4.7 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 5.44 (s, 2H), 3.90 (s, 3H),

3.75 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 1C is less we observed. 160.1, 158.6, 148.5, 144.0, 142.0, 132.1, 130.2, 129.0, 128.3, 123.5, 123.4, 117.1, 113.8, 113.7, 55.3, 55.2, 46.1. HRMS calcd. for $C_{22}H_{19}IN_2O_2$(M+H$^+$): 471.0569 found : 471.0581.

4.2.1. General procedure for the synthesis of C3 arylated pyrrolo[2,3-b]pyridine and its derivatives.

To a sealed tube containing dry DMF, catalyst and ligand 20 mol % each were added under nitrogen atmosphere. After stirring the reaction mixture for 5 minutes at room temperature, 3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo[2,3-*b*]pyridine **1** (0.5 mmol), aryl boronic acid (1.2 equiv., 0.6 mmol) and DABSO (1.5 equiv., 0.75 mmol) were added. The reaction mixture was heated at 100°C in the heating bath under nitrogen atmosphere. When the TLC indicated the total consumption of starting material, the reaction mixture was allowed to cool at ambient temperature. The reaction mixture was quenched with 10 mL of cold water and was extracted with ethyl acetate (50 mL X 3). Organic layer was washed with brine. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the desired products (**4a**-**4zf**).

*4.2.2. 1-(4-methoxybenzyl)-3-((4-methoxyphenyl) sulfonyl)-1H-pyrrolo[2,3-b]pyridine (**4a**)*

Yield : 110 mg (54%); Peach color solid; mp 122-123 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.45-8.44 (m, 1H), 8.21 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.92 (d, *J* = 8.9 Hz, 2H), 7.84 (s, 1H), 7.26-7.23 (m, 3H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.43 (s, 2H), 3.83 (s, 3H), 3.81 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 162.9, 159.6, 147.5, 144.8, 134.7, 131.7, 129.7, 128.9, 128.2, 127.6, 118.3, 116.8, 115.1, 114.4, 114.3, 55.6, 55.3, 48.1. IR ν_{max} (KBr): 3096, 2940, 2837, 1595, 1514, 1496, 1394, 1295 (SO_2), 1258, 1143 (SO_2), 1081, 1027, 676, 584. HRMS calcd. for $C_{22}H_{21}N_2O_4S$ (M+H$^+$): 409.1222. found: 409.1218.

*4.2.3.-1-(4-methoxybenzyl)-3-tosyl-1H-pyrrolo[2,3-b]pyridine (**4b**)*

Yield= 117.6 mg (60%); light yellow solid; mp = 126-127 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.44 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.23 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.87 (d, *J* =8.3 Hz, 2H), 7.85 (s, 1H), 7.28-7.25 (m, 6H, one peak of $CDCl_3$), 6.90-6.88 (m, 2H), 5.43 (s, 2H), 3.82 (s, 3H), 2.38(s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.6, 147.5, 144.9, 143.6, 140.1, 132.0, 129.7, 129.7, 128.3, 127.5, 126.7, 118.4, 116.9, 114.7, 114.4, 55.3, 48.2, 21.5.IR ν_{max} (KBr): 3101, 2937, 2837, 1515, 1392, 1330 (SO_2), 1243, 1145 (SO_2), 1080, 1025, 673, 576. HRMS calcd. for $C_{22}H_{21}N_2O_3S$ (M+H$^+$).: 393.1273. found: 393.1266.

*4.2.4. 3-(3,5(bis(trifluoromethyl)phenyl)sulfonyl)-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridine (**4c**)*

Yield= 115.6 m (45%); peach color solid; mp = 169-170 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.51 (dd, *J* = 4.6, 1.1 Hz, 1H), 8.42 (s, 2H), 8.25 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.02 (s, 1H), 7.93 (s, 1H), 7.34 (dd, *J* =8.0, 4.7 Hz, 1H), 7.27 (d,*J* = 8.2 Hz, 2H), 6.91 (d, *J* =8.6 Hz, 2H), 5.48 (s, 2H), 3.83 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.8, 147.6, 145.9, 145.5, 133.3, 132.9 (q, *J* = 34.3 Hz, 1C), 129.8, 127.8, 127.0, 126.98-126.93 (m, 1C), 126.3-126.2 (m, 1C), 122.4 (d, *J* = 271.4 Hz, 1C), 119.1, 116.8, 114.5, 112.2, 55.3, 48.5.IR ν_{max} (KBr): 3119, 3072, 2843, 1515, 1359, 1309 (SO_2), 1277, 1179, 1145 (SO_2), 1106, 1089, 630, 620. HRMS calcd. for $C_{23}H_{17}F_6N_2O_3S$ (M+H$^+$) :515.0864. found : 515.0864.

*4.2.5. 1-(4-methoxybenzyl)-3-(naphtalen-1-ylsulfonyl)-1H-pyrrolo[2,3-b]pyridine (**4d**)*

Yield = 137mg (64%), white solid, mp = 124-125 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.46-8.44 (m, 2H), 7.88-7.85 (m, 2H), 7.62-7.59 (m, 2H), 7.57-7.55 (m, 1H), 7.53 (s, 1H), 7.29-7.28 (m, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.12 (dd, *J* = 7.8, 4.7 Hz, 1H), 6.94 (dd, *J* = 7.35, 0.9 Hz, 2H), 6.91-6.89 (m, 2H), 5.52 (s, 2H), 3.82 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.3, 148.3, 144.0, 135.9, 134.1, 133.7, 130.7, 129.3, 128.9, 128.4, 128.0, 126.2, 126.1, 125.6, 125.5, 123.9, 123.5, 122.1, 116.8, 114.2, 99.7, 55.3, 47.7.IR ν_{max} (KBr): 2983, 2931, 2803, 1510, 1414, 1300 (SO_2), 1251, 1173, 1161 (SO_2), 1032, 793, 767, 550. MALDI-TOF calcd. for $C_{25}H_{20}LiN_2O_3S$ (M+Li$^+$): 435.1355. found : 435.0511.

*4.2.6. 3-((4,6-dihydropyren-1-yl)sulfonyl)-1-(4-methoxy benzyl)-1H-pyrrolo[2,3-b]pyridine (**4e**)*

Yield= 88 mg (35%), yellow solid, mp = 118-119 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.72 (d, *J* = 9.1 Hz, 1H), 8.44 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.23-8.17 (m, 3H), 8.04-8.00 (m, 2H), 7.95 (d, *J* = 8.9 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.85 (dd, *J* = 7.8, 1.4 Hz, 1H),7.86 (s, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.30 (d, *J* = 8.6 Hz, 2H), 7.08 (dd, *J* = 7.8, 4.7 Hz, 1H), 6.91-6.90 (m 2H), 5.53 (s, 2H), 3.82 (s, 3H), 3.74 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.3,148.4, 144.0, 133.9, 133.2, 131.5, 131.1, 129.3, 129.1, 129.0, 128.0, 127.6, 127.3, 126.7, 126.1, 125.1, 125.0, 124.9, 124.9, 124.6, 123.3, 122.1, 116.9, 114.2, 100.6, 55.3, 47.7.IR ν_{max} (KBr): 3118, 2988, 2948, 1507, 1414, 1289 (SO_2), 1246, 1178, 1159 (SO_2), 1030, 843, 768, 711. MALDI-TOF calcd. for $C_{31}H_{25}N_2O_3S$ (M+H$^+$): 505.1586. found : 506.1168.

*4.2.7. 5-bromo-1-(4-methoxybenzyl)-3-(pyridin-4-ylsulfonyl)-1H-pyrrolo[2,3-b]pyridine(**4f**)*

Yield= 123 mg (54%); peach color solid; mp = 135-136 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.82 (dd, *J* = 4.4, 1.5 Hz, 2H), 8.51 (d, *J*= 2.1 Hz, 1H), 8.38 (d, *J* = 2.1 Hz, 1H), 7.87 (s, 1H), 7.78 (dd, *J* = 4.3, 1.6 Hz, 2H), 7.28-7.25 (m, 2H), 6.89 (dd, *J* = 8.5, 1.8 Hz, 2H), 5.41 (s, 2H), 3.82 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): we observed one carbon peak less in spectra, 159.9, 151.2, 146.3, 145.9, 134.1, 130.2, 129.8, 126.7, 119.6, 118.3, 115.2, 114.6, 112.0, 55.3, 48.7. IR ν_{max} (KBr): 3143, 3036, 2930, 2831, 1513, 1397, 1322 (SO_2), 1245, 1171, 1146 (SO_2), 1090, 1028, 808, 725, 619, 597. HRMS calcd. for $C_{20}H_{17}BrN_3O_3S$ (M+H$^+$): 458.0174. found : 458.0192.

*4.2.8. 5-bromo-1-(4-methoxybenzyl)-3-(thiophen-3-ylsulfonyl)-1H-pyrrolo[2,3-b]pyridine(**4g**)*

Yield = 64 mg (28%); light orange solid; mp = 164-165 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.47 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.24 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.10 (dd, *J* = 2.6, 1.8 Hz, 1H), 7.86 (s, 1H), 7.35-7.34 (m, 2H), 7.28-7.26 (m, 3H, one peak of $CDCl_3$), 6.89 (d, *J* = 8.6 Hz, 2H), 5.45 (s, 2H), 3.82 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.7, 149.0, 147.5, 145.0, 143.7, 132.1, 130.1, 129.7, 128.2, 128.1, 127.4, 125.3, 118.5, 116.9, 114.4, 55.3,

48.2.IR ν_{max} (KBr): 3112, 2959, 2933, 1512, 1416, 1389, 1305 (SO_2), 1243, 1164, 1145 (SO_2), 1088, 1029, 785, 771, 658, 630, 612. HRMS calcd. for $C_{19}H_{17}BrN_2O_3S_2(M+H^+)$:462.9786. found: 462.9806.

*4.2.9. 5-bromo-1-(4-methoxybenzyl)-3-(naphthalene-2-ylsulfonyl)-1H-pyrrolo[2,3-b]pyridine(**4h**)*

Yield= 170.6 mg (68%); light yellow solid; mp = 186-187 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.63-8.59 (m, 2H), 8.46 (d, *J* = 3.6 Hz, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.93-7.86 (m, 4H), 7.65-7.60 (m, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 7.9 Hz, 2H), 5.39 (s, 2H), 3.81 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.7, 150.5, 145.8, 139.5, 136.1, 134.9, 133.3, 132.2, 130.4, 129.7, 129.7, 129.4, 129.0, 127.9, 127.8, 127.6, 122.0, 118.3, 114.7, 114.5, 114.0, 55.3, 48.5.IR ν_{max} (KBr): 3086, 2950, 2926, 1510, 1394, 1307 (SO_2), 1298, 1249, 1169, 1145 (SO_2), 1128, 1072, 805, 681, 655, 641. HRMS calcd.for $C_{25}H_{20}BrN_2O_3S(M+H^+)$: 507.0378. found : 507.0392.

*4.2.10. 3-(anthracen-2-ylsulfonyl)-5-bromo-1-(4-methoxy benzyl)-1H-pyrrolo[2,3-b]pyridine (**4i**)*

Yield = 196mg (71%), light yellow solid, mp = 210-211 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.80 (s, 1H), 8.66-8.61 (m, 1H), 8.47-8.43 (m, 3H), 8.06-8.04 (m, 3H), 7.93-7.83 (m, 1H), 7.77-7.75 (m, 1H), 7.57 (s, 2H), 7.28-7.24 (m, 2H), 6.90-6.88 (m, 2H), 5.40 (s, 2H), 3.81 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.8, 145.9, 138.7, 133.4, 133.3, 132.4, 131.7, 130.4, 130.2, 129.7, 129.6, 129.0, 128.9, 128.4, 128.2, 127.0, 126.6, 126.4, 120.6, 118.4, 114.8, 114.5, 113.9, 55.3, 48.5, 29.7 (acetone).IR ν_{max} (KBr): 2923, 1511, 1314 (SO_2), 1249, 1171, 1136 (SO_2), 828, 721, 642. 623, 556. MALDI-TOF calcd. for $C_{29}H_{22}BrN_2O_3S$ $(M+H^+)$: 557.0535. found : 557.0112.

*4.2.11. 6-chloro-1-(4-methoxybenzyl)-3-(phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine(**4j**)* :

Yield= 160.6 mg (78%); light brown solid; mp = 132-133 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.16 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.77 (s, 1H), 7.53 (t, *J* = 7.3 Hz, 1H), 7.48-7.47 (m, 2H),7.25 (d, *J* = 8.3 Hz, 3H), 6.89 (d, *J* = 8.5 Hz, 2H), 5.36 (s, 2H), 3.81 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.8, 146.7, 146.5, 142.7, 132.9, 132.1, 130.6, 130.0, 129.2, 126.8, 126.7, 119.0, 115.5, 115.0, 114.5, 55.3, 48.4.IR ν_{max} (KBr): 3116, 2949, 2923, 1515, 1409, 1303 (SO_2), 1250, 1162, 1147 (SO_2), 1078, 1031, 725, 621, 594. HRMS calcd. for $C_{21}H_{18}ClN_2O_3S$ $(M+H^+)$: 413.0727. found : 413.0748.

*4.2.12. 6-chloro-1-(4-methoxybenzyl)-3-(m-tolylsulfonyl)-1H-pyrrolo[2,3-b]pyridine (**4k**)*

Yield= 121 mg (57%); light brown solid; mp = 91-92 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.17 (d, *J* = 8.3 Hz, 1H), 7.819-7.815 (m, 1H), 7.77-7.76 (m, 2H), 7.38-7.32 (m, 2H),7.28-7.25 (m, 3H), 6.89 (d, *J* = 8.5 Hz, 2H), 5.38 (s, 2H), 3.81 (s, 3H), 2.39 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.8, 149.0, 146.7, 146.5, 142.6, 139.5, 133.7, 132.1, 130.6, 129.9, 129.1, 127.0, 123.8, 118.9, 115.5, 115.1, 114.5, 55.3, 48.4, 21.3.IR ν_{max} (KBr): 3135, 3017, 2963, 2839, 1514, 1411, 1384, 1303 (SO_2), 1246, 1162, 1145 (SO_2), 1117, 1077, 1032, 768, 699, 630, 601. HRMS calcd. for $C_{22}H_{20}ClN_2O_3S$ $(M+H^+)$: 427.0883. found : 427.0887.

*4.2.13. 6-chloro-3-((4-fluorophenyl)sulfonyl)-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridine (**4l**)*

Yield= 111.8 mg (52%); off white solid; mp = 144-145 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.16-8.15 (m, 1H), 7.99-7.96 (m, 2H), 7.78 (s, 1H), 7.28-7.26 (m, 3H), 7.16-7.14 (m, 3H, one peak extra due to $CDCl_3$), 6.91-6.89 (m, 2H), 5.38 (s, 2H), 3.83 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 165.2 (d, *J* = 253.9 Hz, 1C), 159.8, 146.9, 146.5, 138.8 (d, *J* = 3.1 Hz, 1C), 132.1, 130.5, 130.0, 129.5 (d, *J* = 9.4 Hz, 1C), 126.8, 119.1, 116.5 (d, *J* = 22.5 Hz, 1C), 115.3, 114.9, 114.5, 55.3, 48.5, 30.6 (acetone).IR ν_{max} (KBr): 3115, 3079, 2948, 2831, 1612, 1589, 1515, 1315(SO_2), 1289, 1251, 1148(SO_2), 1078, 1033, 837, 816, 676, 591, 529. HRMS calcd. for $C_{21}H_{17}ClFN_2O_3S$ $(M+H^+)$: 431.0632. found: 431.0636.

*4.2.14. 6-chloro-1-(4-methoxybenzyl)-3-((4-trifluoro methoxy)phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine (**4m**)*

Yield= 114 mg (46%); white solid; mp = 114-115 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.18 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 8.8 Hz, 2H), 7.79 (s, 1H), 7.32-7.27 (m, 5H), 6.91 (d, *J* = 8.6 Hz, 2H), 5.39 (s, 2H), 3.83 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) We are getting one less carbon peak here δ(ppm): 159.9, 152.2, 147.0, 146.5, 141.0, 132.3, 130.5, 130.0, 128.9, 126.7, 121.0, 119.2, 115.4, 114.5, 114.4, 55.3, 48.5. IR ν_{max} (KBr): 3076, 2966, 2846, 1514, 1324 (SO_2), 1263, 1214, 1159, 1149 (SO_2), 1080, 1033, 808, 629, 596. HRMS calcd. for $C_{22}H_{17}ClF_3N_2O_4S$ $(M+H^+)$: 497.0550. found : 497.0568.

*4.2.15. (E)-6-chloro-1-(4-methoxybenzyl)-3-((4-methoxy styryl)sulfonyl)-1H-pyrrolo[2,3-b]pyridine **(4n)***

Yield = 98 mg (42%); white solid; mp = 169-170 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.16 (d, *J* = 8.3 Hz, 1H), 7.75 (s, 1H), 7.65 (d, *J* = 15.2 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.29 (dd, *J* = 11.2, 8.6 Hz, 3H), 6.92-6.88 (m, 4H), 6.76 (d, *J* = 15.2 Hz, 1H), 5.40 (s, 2H), 3.84 (s, 3H), 3.82 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 161.9, 159.8, 146.7, 146.5, 140.8, 132.1, 130.6, 130.2, 130.1, 127.0, 125.6, 124.9, 118.8, 115.5, 114.5, 114.4, 114.4, 55.4, 55.3, 48.4. IR ν_{max} (KBr): 3135, 3052, 2949, 2833, 1601, 1513, 1305 (SO_2), 1287, 1259, 1159 (SO_2), 1110, 838, 628, 592. HRMS calcd. for $C_{24}H_{22}ClN_2O_4S$: 469.0989. found: 469.0998.

*4.2.16. 4-((4-chloro-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)sulfonyl)benzonitrile (**4o**)*

Yield= 76 mg (35%); white solid; mp = 172-173 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.34 (d, *J* = 5.1 Hz, 1H), 8.1.8 (s, 1H), 8.05 (d, *J* = 8.5 Hz, 2H),7.78 (d, *J* = 8.4 Hz, 2H), 7.31-7.28 (m, 3H, one extra peak due to $CDCl_3$), 7.23 (d, *J* = 5.1 Hz, 1H), 6.92 (d, *J* =8.5 Hz, 2H), 5.48 (s, 2H), 3.83 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.9, 149.2, 146.9, 145.4, 136.4, 136.1, 132.7, 129.8, 128.2, 126.8, 119.9, 117.3, 116.3, 115.1, 114.6, 112.6, 55.3, 48.9.IR ν_{max} (KBr): 3117, 2957, 2928, 2831, 2230, 1514, 1388, 1303 (SO_2), 1249, 1167, 1143 (SO_2), 831, 647, 599. HRMS calcd. for $C_{22}H_{17}ClN_3O_3S(M+H^+)$: 438.0679. found : 438.0685.

*4.2.17. 6-methoxy-1-(4-methoxybenzyl)-3-(phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine (**4p**)*

Yield= 91.8 mg (45%); peach color solid; mp = 144-145 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.07(d, *J* = 8.6 Hz, 1H), 7.98-7.97 (m, 2H), 7.67 (s, 1H), 7.54 -7.50 (m, 1H), 7.49-7.45 (m, 2H), 7.29-7.27 (m, 2H), 6.90-6.87 (m, 2H), 6.72 (d, *J* =8.6 Hz, 1H), 5.33 (s, 2H), 4.00 (s, 3H), 3.82 (s,

3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 161.9, 159.6, 145.4, 143.2, 132.5, 130.8, 129.7, 129.0, 128.9, 127.9, 126.6, 114.7, 114.3, 110.6, 107.1, 55.3, 53.6, 48.3.IR ν_{max} (KBr): 3125, 3005, 2977, 2942, 2839, 1604, 1511, 1413, 1302 (SO_2), 1270, 1242, 1147 (SO_2), 1026, 722, 591. HRMS calcd. for $C_{22}H_{21}N_2O_4S$ ($M+H^+$): 409.1222. found: 409.1221.

*4.2.18. 3-((4-fluorophenyl)sulfonyl)-6-methoxy-1-(4-methoxy benzyl)-1H-pyrrolo[2,3-b]pyridine (**4q**)*

Yield = 142.7 mg (67%); off white solid; mp = 173-174 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.04 (d, *J* = 8.6 Hz, 1H), 7.98 (dd, *J* = 8.6, 5.1 Hz, 2H), 7.66 (s, 1H), 7.29-7.27 (m, 2H), 7.14 (t, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.73 (d, *J* = 8.6 Hz, 1H), 5.33 (s, 2H), 4.00 (s, 3H), 3.81 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 165.0 (d, *J* = 253.1 Hz, 1C), 161.9, 159.6, 145.4, 139.4 (d, *J* = 3.1 Hz, 1C), 130.6, 129.7, 129.3 (d, *J* = 9.3 Hz, 1C), 128.9, 127.8, 116.3 (d, *J* = 22.4 Hz, 1C), 114.5, 114.3, 110.5, 107.3, 55.3, 53.6, 48.3. IR ν_{max} (KBr): 3143, 3036, 2930, 2833, 1513, 1397, 1322 (SO_2), 1245, 1171, 1146 (SO_2), 1090, 1028, 808, 619, 597. HRMS calcd. for $C_{22}H_{20}FN_2O_4S(M+H^+)$:427.1128. found : 427.1120.

*4.2.19. 6-methoxy-1-(4-methoxybenzyl)-3-((3-nitrophenyl) sulfonyl)-1H-pyrrolo[2,3-b]pyridine (**4r**)*

Yield = 122 mg (54%); light orange solid; mp = 180-181 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.06 (d, *J* = 8.6 Hz, 1H), 7.64 (s, 1H), 7.32-7.27 (m, 4H, one peak extra due to $CDCl_3$), 7.25 (t, *J* = 2.0 Hz, 1H), 7.21 (t, *J* = 7.9 Hz, 1H), 6.89-6.86 (m, 2H), 6.78-6.76 (m, 1H), 6.71 (d, *J* = 8.6 Hz, 1H), 5.32 (s, 2H), 4.00 (s, 3H), 3.81 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 161.8, 159.5, 147.0, 145.3, 144.0, 130.9, 129.9, 129.7, 128.8, 127.9, 118.8, 116.3, 114.7, 114.2, 112.3, 110.7, 107.0, 55.3, 53.5, 48.2.IR νmax (KBr): 3446, 3360, 3248, 3094, 2952, 2837, 1602, 1513, 1441, 1409, 1293 (SO_2), 1272, 1243, 1139 (SO_2), 1023, 706, 644, 415. HRMS calcd. for $C_{22}H_{20}N_3O_6S(M+H^+)$: 454.1072. found : not observed.

*4.2.20. 3-((4-bromophenyl)sulfonyl)-6-methoxy-1-(4-methoxy benzyl)-1H-pyrrolo[2,3-b]pyridine (**4s**)*

Yield = 124 mg (51%); white solid; mp = 123-124 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.04 (d, *J* = 8.6 Hz, 1H), 7.83-7.81 (m, 2H), 7.68-7.59 (m, 3H), 7.29 – 7.27 (m, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.73 (d, *J* = 8.6 Hz, 1H), 5.33 (s, 2H), 4.00 (s, 3H), 3.81 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 162.0, 159.6, 145.4, 142.3, 138.3, 132.3, 130.6, 129.8, 129.0, 128.2, 128.1, 127.7, 114.3, 110.5, 107.4, 55.3, 53.6, 48.3.IR ν_{max} (KBr): 3133, 3009, 2945, 2825, 1601, 1574, 1413, 1387, 1311 (SO_2), 1272, 1249, 1147 (SO_2), 1028, 818, 630, 586. HRMS calcd. for $C_{22}H_{20}BrN_2O_4S$ ($M+H^+$): 487.0327. found : 487.0341.

*4.2.21. 6-methoxy-1-(4-methoxybenzyl)-3-(((4-methylthio) phenyl)sulfonyl)-1H-pyrrolo[2,3-b]pyridine (**4t**)*

Yield = 129.4 mg (57%); light orange solid; mp = 132-133 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.05 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 2H), 7.64 (s, 1H), 7.26 (dd, *J* = 10.6, 8.7 Hz, 5H, one peak of $CDCl_3$ extra), 6.89 (d, *J* = 8.6 Hz, 2H), 6.71 (d, *J* = 8.6 Hz, 1H), 5.32 (s, 2H), 4.00 (s, 3H), 3.81 (s, 3H), 2.48 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 161.9, 159.5, 145.6, 145.4, 139.0, 130.7, 129.7, 128.6, 127.9, 127.0, 125.4, 115.0, 114.3, 110.5, 107.1, 55.3, 53.6, 48.2, 14.7.IR ν_{max} (KBr): 3134, 3060, 2955, 1600, 1577, 1510, 1414, 1309 (SO_2), 1273, 1245, 1148 (SO_2), 1091, 1078, 816, 642, 584. HRMS calcd. for $C_{23}H_{23}N_2O_4S_2(M+H^+)$: 455.1099. found : 455.1098.

*4.2.22. 4-((6-methoxy-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)sulfonyl)benzonitrile (**4u**)*

Yield = 127.7 mg (59%); white solid; mp = 185-186 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.07-8.04 (m, 3H), 7.77-7.75 (m, 2H), 7.68 (s, 1H), 7.29-7.27 (m, 2H), 6.90-6.88 (m, 2H), 6.75 (d, *J* = 8.6 Hz, 1H), 5.34 (s, 2H), 4.01 (s, 3H), 3.82 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 162.1, 159.7, 147.4, 145.5, 132.9, 130.5, 129.8, 129.6, 127.5, 127.2, 117.3, 116.2, 114.3, 113.1, 110.5, 107.7, 55.3, 53.7, 48.6.IR ν_{max} (KBr): 3124, 2955, 2840, 2230, 1604, 1514, 1410, 1299 (SO_2), 1274, 1248, 1145 (SO_2), 1031, 822, 663, 560. HRMS calcd.for $C_{23}H_{20}N_3O_4S(M+H^+)$. :434.1175. found: 434.1175.

*4.2.23. 6-methoxy-1-(4-methoxybenzyl)-3-((3,4,5-trimethoxy phenyl)sulfonyl)-1H-pyrrolo[2,3-b]pyridine (**4v**)*

yield = 159 mg (64%);White solid; mp = 175-176 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.08 (d, *J* = 8.6 Hz, 1H), 7.66 (s, 1H), 7.27 (d, *J* = 8.9 Hz, 2H), 7.18 (s, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.73 (d, *J* = 8.6 Hz, 1H), 5.34 (s, 2H), 4.00 (s, 3H), 3.86 (s, 6H), 3.85 (s, 3H), 3.81 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 161.9, 159.6, 153.3, 145.4, 141.4, 138.0, 130.7, 129.7, 128.7, 128.0, 114.8, 114.2, 110.5, 107.2, 103.9, 60.9, 56.3, 55.3, 53.6, 48.2. IR ν_{max} (KBr): 3116, 2947, 2836, 1600, 1515, 1496, 1413, 1307 (SO_2), 1254, 1163, 1139 (SO_2), 1123, 1011, 649, 629. HRMS calcd.for $C_{25}H_{27}N_2O_7S(M+H^+)$: 499.1539. found : 499.1537.

*4.2.24. 3-((6-methoxy-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)sulfonyl)phenol (**4w**)*

Yield = 112 mg (53%); white solid; mp = 177-178 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.06 (s, 1H), 8.04 (d, *J* = 8.6 Hz, 1H), 8.02 (s, 1H, DMF), 7.65 (s, 1H), 7.53 (t, *J* = 2.0 Hz, 1H),7.46-7.44 (m, 1H), 7.29-7.25 (m, 3H), 7.01 (dd, *J* = 7.4, 2.4 Hz, 1H), 6.87-6.85 (m, 2H), 6.68 (d, *J* = 8.6 Hz, 1H), 5.30 (s, 2H), 3.98 (s, 3H), 3.80 (s, 3H), 2.98 (s, 3H, DMF), 2.91 (s, 3H, DMF).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 162.0 (DMF), 161.8, 159.5 157.2, 145.4, 144.0, 130.8, 130.2, 129.7, 129.0, 127.9, 120.1, 118.0, 114.4, 114.2, 113.5, 110.6, 107.1, 55.3, 53.6, 48.2, 36.7 (DMF), 31.6 (DMF).IR ν_{max} (KBr): 3340, 3102, 2928, 1602, 1514, 1443, 1411, 1306 (SO_2), 1270, 1137 (SO_2), 706, 686, 623. HRMS calcd. for $C_{22}H_{21}N_2O_5S$ ($M+H^+$): 425.1171. found : 425.1165.

*4.2.25 3-((6-methoxy-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)sulfonyl)benzaldehyde (**4x**)*

Yield = 128.6 mg (59%); light orange solid; mp = 157-158 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 10.04 (s, 1H), 8.44 (s, 1H), 8.23 (d, *J* = 7.7 Hz, 1H), 8.07 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 7.5 Hz, 1H),7.71 (s, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.74 (d, *J* = 8.6 Hz, 1H), 5.34 (s, 2H), 4.00 (s, 3H), 3.82 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 190.4, 162.0, 159.6, 145.5, 144.8, 136.9, 132.9, 131.9, 130.6, 130.0, 129.8, 129.4, 127.8, 127.7, 114.3, 113.7, 110.5, 107.5, 55.3, 53.6, 48.2.IR ν_{max} (KBr): 3129, 2951, 2834, 2734, 1705, 1513, 1389, 1307 (SO_2), 1281, 1249, 1156, 1141 (SO_2), 1013, 820, 620, 601. HRMS calcd. for $C_{23}H_{21}N_2O_5S$ ($M+H^+$) : 437.1171. found : 437.1170.

*4.2.26 3-(benzo[d][1,3]dioxol-5-ylsulfonyl)-6-methoxy-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridine (**4y**)*

Yield = 110 mg (49%); white solid; mp = 155-156 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.04 (d, *J* = 8.6 Hz, 1H), 7.63 (s, 1H), 7.58 (dd, *J* = 8.2, 1.8 Hz, 1H),7.35 (d, *J* = 1.8 Hz, 1H), 7.29 (d, *J* = 2.5 Hz, 1H), 7.27 (s, 1H), 6.88 (m, 2H), 6.85 (d, *J* =8.2 Hz, 1H), 6.72 (d, *J* =8.6 Hz, 1H), 6.03 (s, 2H), 5.32 (s, 2H), 4.00 (s, 3H), 3.82 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): (one carbon might be merged here) 161.9, 159.5, 151.3, 148.1, 145.4, 136.7, 130.8, 129.7, 128.5, 127.9, 122.3, 115.1, 114.3, 110.5, 108.3, 107.1, 102.2, 55.3, 53.6, 48.2.IR ν_{max} (KBr): 3125, 3066, 2904, 1514, 1480, 1414, 1307 (SO_2), 1276, 1250, 1157 (SO_2), 1105, 1035, 818, 706, 616, 522. HRMS calcd. for $C_{23}H_{21}N_2O_6S$ ($M+H^+$): 453.1120. found: 453.1115.

4.2.27 3-((2,3-dihyrobenzo[b][1,4]dioxin-6-yl)sulfonyl)-6-methoxy-1-(4-methoxybenzyl)-1H-pyrrolo[2,3-b]pyridine ***(4z)***

Yield = 125.8 mg (54%); light orange solid; mp = 152-153 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.05 (d, *J* = 8.6 Hz, 1H), 7.62 (s, 1H), 7.48 (s, 1H), 7.46 (d, *J* = 2.0 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 2H), 6.92-6.87 (m, 3H), 6.71 (d, *J* = 8.6 Hz, 1H), 5.31 (s, 2H), 4.27- 4.24 (m, 4H), 3.99 (s, 3H), 3.81 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 161.8, 159.5, 147.3, 145.4, 143.5, 135.8, 130.8, 129.7, 128.5, 127.9, 120.4, 117.8, 116.3, 115.2, 114.3, 110.5, 107.0, 64.4, 64.1, 55.3, 53.6, 48.2.IR ν_{max} (KBr): 3115, 2936, 2884, 2840, 1605, 1516, 1491, 1303 (SO_2), 1277, 1252, 1144 (SO_2), 1111, 1073, 1023, 876, 828, 652. HRMS calcd. for $C_{24}H_{23}N_2O_6S$ ($M+H^+$): 467.1277. found: 467.1275

4.2.28. 1-(4-methoxybenzyl)-5-(4-methoxybenzyl)-3-((4-methoxyphenyl)sulfonyl)-1H-pyrrolo[2,3-b]pyridin ***(4za)***

Yield = 120.7 mg (47%); light brown solid; mp = 165-166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.63 (d, *J* = 2.1 Hz, 1H), 8.33 (d, *J* = 2.1 Hz, 1H), 7.95-7.93 (m, 2H), 7.85 (s, 1H), 7.57-7.55 (m, 2H), 7.29-7.27 (m, 2H), 7.06-7.05 (m, 2H), 6.95-6.93 (m, 2H), 6.91-6.89 (m, 2H), 5.44 (s, 2H), 3.90 (s, 3H), 3.82 (s, 6H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 162.9, 159.6, 159.4, 146.7, 144.1, 134.7, 132.2, 132.0, 131.0, 129.7, 128.8, 128.6, 127.6, 125.9, 116.8, 115.1, 114.5, 114.4, 114.3, 55.6, 55.4, 55.3, 48.3.IR ν_{max} (KBr): 3111, 2934, 2831, 1596, 1514, 1320, 1296 (SO_2), 1257, 1178, 1141 (SO_2), 831, 674, 596. HRMS calcd. for $C_{29}H_{27}N_2O_5S$ ($M+H^+$): 515.1640. found : 515.1636.

4.2.29. 1-(4-methoxybenzyl)-5-(4-methoxybenzyl)-3-(o-tolylsulfonyl)-1H-pyrrolo[2,3-b]pyridine ***(4zb)***

Yield = 87 mg (35%); white solid; mp = 127-128 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.62 (d, *J* = 2.0 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 8.14 (d, *J* = 1.9 Hz, 1H), 7.92 (s, 1H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.46-7.43 (m, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.29-7.28 (m, 3H, one peak of $CDCl_3$),7.22 (d, *J* = 7.4 Hz, 1H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 5.49 (s, 2H), 3.89 (s, 3H), 3.83 (s, 3H), 2.54 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.6, 159.4, 146.6, 144.2, 140.4, 137.5, 133.1, 133.1, 132.7, 132.0, 130.9, 129.6, 128.6, 128.4, 127.6, 126.5, 125.8, 117.0, 114.5, 114.4, 113.5, 55.4, 55.3, 48.3, 20.0.IR ν_{max} (KBr): 3105, 2931, 2828, 1609, 1513, 1302 (SO_2), 1240, 1178, 1162, 1147 (SO_2), 1030, 827, 693, 605. HRMS calcd.for $C_{29}H_{27}N_2O_4S$ ($M+H^+$): 499.1692. found : 499.1701.

4.2.30 3-(benzo[d][1,3]dioxol-5-ylsulfonyl)-1-(4-methoxy benzyl)-5-(4-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridine ***(4zc)***

Yield = 145 mg (55%); light orange solid; mp = 181-182 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.64 (d, *J* = 1.9 Hz, 1H), 8.31 (d, *J* = 1.9 Hz, 1H), 7.84 (s, 1H), 7.61 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.37 (d, *J* = 1.5 Hz, 1H), 7.29-7.28 (m, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.03 (s, 2H), 5.45 (s, 2H), 3.90 (s, 3H), 3.83 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.7, 159.4, 151.4, 148.2, 146.7, 144.2, 136.5, 132.4, 132.1, 130.9, 129.7, 128.7, 127.5, 125.8, 122.4, 116.8, 114.7, 114.5, 114.4, 108.4, 107.0, 102.2, 55.4, 55.3, 48.3.IR ν_{max} (KBr): 3100, 2962, 2831, 1609, 1512, 1482, 1312 (SO_2), 1247, 1163, 1134 (SO_2), 1034, 834, 620, 554. HRMS calcd. for $C_{29}H_{25}N_2O_6S$ ($M+H^+$): 529.1433. found: 529.1456.

4.2.31 1-(4-methoxybenzyl)-4-tosyl-1H-pyrrolo[2,3-b] pyridine ***(4zd)***

Yield = 98mg (50%); light yellow solid; mp = 130-131 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.50 (d, *J* = 5.0 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 5.0 Hz, 1H), 7.37 (d, *J* = 3.6 Hz, 1H), 7.30-7.28 (m, 2H), 7.20-7.18 (m, 2H), 6.95 (d, *J* = 3.5 Hz, 1H), 6.86-6.83 (m, 2H), 5.45 (s, 2H), 3.79 (s, 3H), 2.39 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 159.3, 149.0, 144.5, 142.7, 140.0, 138.0, 130.9, 129.8, 129.2, 128.8, 127.8, 116.2, 114.2, 114.1, 99.6, 55.2, 47.8, 21.5.IR ν_{max} (KBr): 2923, 2853, 1514, 1304 (SO_2), 1274, 1249, 1144 (SO_2), 1082, 681, 645, 558. HRMS calcd. for $C_{22}H_{21}N_2O_3S$ ($M+H^+$): 393.1275. found: 393.1256.

4.2.32 1-(4-methoxybenzyl)-3-(((4-methylthio)phenyl) sulfonyl)-5-(p-tolylethynyl)-1H-pyrrolo[2,3-b]pyridine ***(4ze)***

Yield = 137 mg (51%); brown solid; mp = 184-185 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.59 (s, 1H), 8.37 (s, 1H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.84 (s, 1H), 7.50 (d, *J* = 7.7 Hz, 2H), 7.31-7.26 (m, 5H, one peak of $CDCl_3$), 7.22 (d, *J* = 7.7 Hz, 2H), 6.92-6.89 (m, 2H), 5.42 (s, 2H), 3.83 (s, 3H), 2.49 (s, 3H), 2.41 (s, 3H). ^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 159.7, 147.8, 146.2, 146.0, 138.8, 138.5, 132.7, 131.5, 130.7 129.8, 129.2, 128.6, 127.2, 127.0, 125.5, 119.7, 116.3, 115.3, 114.8, 114.5, 113.9, 91.5, 86.0, 55.3, 48.4, 29.7 (acetone), 21.6, 14.7.IR ν_{max} (KBr): 3110, 2922, 1513, 1390, 1310 (SO_2), 1254, 1172, 1141 (SO_2), 1089, 816, 755, 646, 615. HRMS calcd.for $C_{31}H_{27}N_2O_3S_2$ ($M+H^+$): 539.1463. found : 539.1448.

4.2.33. (E)-1-(4-methoxybenzyl)-2-(4-methoxyphenyl)-3-((4-methoxystyryl)sulfonyl)-1H-pyrrolo[2,3-b]pyridine ***(4zf)***

Yield = 108 mg (40%); light yellow solid; mp = 142-143 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.56 (d, *J* = 7.8 Hz, 1H), 8.49 (d, *J* = 4.1 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 4H), 7.05 (d, *J* = 15.3 Hz, 1H), 6.92 (d, *J* = 8.5 Hz, 2H),6.86 (t, *J* = 7.6 Hz, 4H), 6.70 (d, *J* = 8.5 Hz, 2H), 6.57 (d, *J* = 15.3 Hz, 1H), 5.34 (s, 2H), 3.87 (s, 3H), 3.83 (s, 3H), 3.74 (s, 3H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ(ppm): 161.6, 160.7, 158.9, 146.6, 144.7, 144.3, 140.2, 132.3, 130.0, 129.2, 129.0, 128.7, 125.8, 125.3, 120.3, 118.6, 118.0, 114.2, 113.7, 113.5, 112.0, 55.4, 55.3, 55.2, 45.6, 30.6 (acetone).IR ν_{max} (KBr): 3113, 3093, 2931, 2835, 1611, 1595, 1514, 1304 (SO_2), 1246, 1174, 1141(SO_2), 1115, 1033, 696, 620. HRMS calcd. for $C_{31}H_{28}ClN_2O_5S$ ($M+H^+$): 541.1797. found : 541.1766.

4.3. General procedure for deprotection of PMB group.

Compound **4j** (82 mg, 0.2 mmol) was taken in a sealed tube and kept it in ice. Added 2 ml TFA neat carefully dropwise and stirred for 5 mins. Added 1.5 equiv. of mesitylene

(36mg, 0.3 mmol), to the tube and stirred at 90° C for 5 h. After the completion of reaction as indicated by TLC, the reaction was quenched by the addition of sat. aq. $NaHCO_3$ solution (10 mL) and diluted with CH_2Cl_2 (5 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (3 x 30 mL). The solvent was removed in vacuum and the crude product was purified by silica flash column chromatography to afford **8** as white powder.

*3-(phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine(**8**)*

Yield = 46mg (80%); white solid; mp = 234-235 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 13.1 (s, 1H), 8.44 (d, *J* = 2.5 Hz, 1H), 8.23 (d, *J* = 8.3 Hz, 1H), 8.02-8.00 (m, 1H), 7.64 -7.63 (m, 1H), 7.60-7.57 (m, 2H), 7.36 (d, *J* = 8.3 Hz, 1H).^{13}C{H} NMR (125 MHz, $CDCl_3$) δ (ppm): 147.5, 145.6, 143.2, 133.6, 133.1, 130.9, 130.0, 126.8, 118.6, 115.2, 114.9. HRMS calcd. for $C_{13}H_{11}N_2O_2S$ ($M+H^+$): 293.0152. found : 293.0178.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at.

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Declaration of interests

✓ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: