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Microwave-assisted chemoselective reaction: a divergent synthesis of pyrazolopyridine derivatives with different substituted patterns

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ABSTRACT

A series of new functionalized pyrazolopyridine derivatives with different substituted patterns were synthesized via microwave-assisted multi-component divergent reactions of aldehydes, 5-aminopyrazoles, and cycloketones by controlling the reaction condition. The procedures are facile, avoiding time-consuming and costly syntheses, tedious work-up, and purifications of precursors as well as protection/deprotection of functional groups. This chemistry provides an efficient and promising synthetic strategy to construction of the pyrazolopyridine skeleton.

1. Introduction

Selectivity is a key issue to be controlled in organic synthesis. In particular, chemoselectivity is synthetically useful because it gives one of several products selectively from the same substrate without the need to separate the product(s) from the product mixture. It continues to be developed as organic synthesis strives for ever-increasing levels of efficiency. As a result, many studies have focused on the chemoselectivity of reactions.[1] In recent years, many reports have dealt with the control of chemoselectivity reactions with metal catalysts,[1a–e] while solvent-dependent chemoselective reactions have been researched in relatively few papers.[1g–i] Therefore, the development of highly solvent-dependent chemoselective reactions remains a challenge.

The pyrazolo[3,4-*b*]pyridine moieties represent important building blocks in both natural and synthetic bioactive compounds,[2] which show anxiolytic,[3] inhibitors of xanthine oxidases,[4] cholesterol formation-inhibiting compounds,[5] treatment of Alzheimer's disease, gastrointestinal diseases, anorexia nervosa, drug and alcohol withdrawal symptoms, drug addiction, and infertility activities.[6] They also act as potent and selective inhibitors of A1 adenosine receptors,[7] phosphodiesterase 4 (PDE4) inhibitors in immune and inflammatory cells,[8] glycogen synthase kinase-3 (GSK-3) inhibitors,[9] kinase inhibitors of p38aas anti-inflammatory drugs.[10] Therefore, the synthesis of this type of compounds has attracted considerable attention.[11] Many pyrazolo[3,4-*b*]pyridines have been synthesized by the reactions of 5-aminopyrazoles, aldehydes, and appropriate cycloketones via various methods.[12] However, most of these compounds belong to pyrazolo[3,4-*b*]pyridines **I** (Fig. 1) with aryl group residing in 4-position of pyridine nucleus. Recently, Chebanov and co-workers presented the similar three-component synthesis of unexpected pyrazolopyridine **II** under strong base condition, and aryl group was also seated on 4-position of pyridine ring in this reaction (Fig. 1).[13] In our previous report, we synthesized polyfunctionalized macrocyclane-fused pyrazolopyridines of type **III** through the Povarov reaction of macrocycloketones in the presence of TFA.[14] However, under base condition the reaction gave complex mixtures instead of type **IV**. In a further study, we found the cyclopentanone was subjected with aldehydes and 5-aminopyrazoles, and a series of new polyfunctionalized pyrazolopyridine derivatives (types **III** and **IV**) with

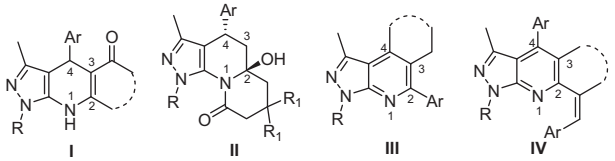

Fig. 1. Different substituted patterns for the condensation of 5-aminopyrazoles, aldehydes, and cycloketones.

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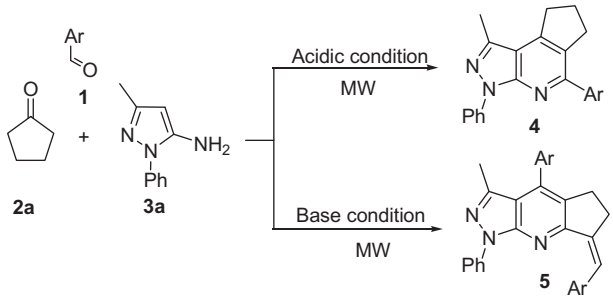
different substituted patterns were synthesized through microwave-assisted divergent reaction. To the best of our knowledge, the synthesis of pyrazolopyridines of type **IV** with strong rigidity and big π-conjugation systems is seldom investigated so far.

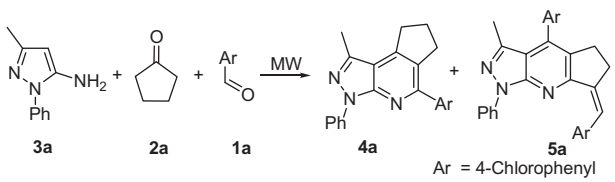
In the past several years, our group have developed various multi-component reactions (MCRs) that can provide easy access to useful functionalized multiple ring structures of chemical and pharmaceutical interest.[14–17] As a continuation of our research devoted to the development of multi-component reactions, we would like to report another new divergent approach to regioselective construction of pyrazolopyridines with different substituted patterns that are of chemical and biomedical importance (Scheme 1). This reaction was achieved from the same starting materials, such as aldehyde, cyclic ketones, and aminopyrazole in different reaction conditions under microwave irradiation.



Scheme 1. Different reaction pathways for the condensation of 5-aminopyrazoles, aldehydes, and cyclic ketones.

2. Results and discussion

We devoted our efforts to the study of the reaction of 4-chlorobenzaldehyde **1a** and cyclopentanone **2a** with 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **3a** as a model reaction (Scheme 2). Experiments were carried out in various solvents, such as toluene, THF, and HOAc. Unfortunately, the reaction scarcely proceeded in toluene and THF. When HOAc was used as the solvent, the reaction proceeded smoothly and the two products **4a** and **5a** were successfully isolated after work-up and column chromatography gave these in 43% and 28% yield, respectively. The structures of **4a** and **5a** were characterized on the basis of their spectra and analytical data. Furthermore, the structural elucidation and attribution of relative stereochemistry were unequivocally determined by X-ray diffraction of single crystals that were obtained by slow evaporation of the solvent, as in the case of **5a** (Fig. 2). Clearly, the three reactants in different molar ratio take part in the multi-component reaction, leading to different substituted patterns on the cyclane-fused pyrazolopyridine framework. It was reasonable to believe that either **4** or **5** may be achieved as the sole product after optimization of the reaction, respectively.



Scheme 2. Optimized condition for three-component reaction.

With this idea in mind, we modified the reaction in Scheme 2 by varying the amount of aldehyde and cyclic ketones in the reaction system. Upon treatment of 4-chlorobenzaldehyde (**1a**) with

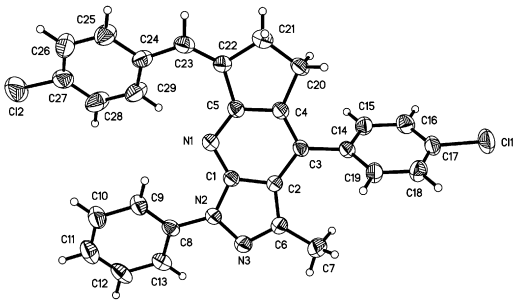


Fig. 2. ORTEP drawing of **5a**.[20]

cyclopentanone (**2a**, 1.5 equiv) and 3-methyl-1-phenyl-1*H*-pyrazol-5-amine (**3a**, 1.0 equiv), the reaction exclusively afforded **4a** as the sole product in 40% yield (Table 1, entry 1). To further optimize reaction conditions, the reaction was performed in HOAc and repeated many times at different temperatures in a sealed vessel under microwave irradiation for 15 min. The yield of product **4a** was increased from 40% to 79% as the temperature varied from 80 °C to 120 °C. Further increase of reaction temperature failed to improve the yield of product **4a** (Table 1, entries 5–6) (Scheme 2). In the following work, a variety of aldehydes **1** were subjected to the reactions under identical conditions (Table 2). It was observed that aldehyde substrates bearing a variety of either electron donating or electron withdrawing functional groups were efficient for the three-component reaction, giving the corresponding cyclopenta[*d*]pyrazolo[3,4-*b*]pyridines **4a**–**g** in high yields (Table 2, entries 1–7). Moreover, the heterocyclic aldehyde, such as thiophene-2-carbaldehyde (Table 2, entry 8) still displayed high reactivity under this standard condition, furnishing thienyl-substituted cyclopenta[*d*]pyrazolo[3,4-*b*]pyridines **4h** in 80% yield (entry 8). In order to determine the scope with respect to the amine component, and to prepare polysubstituted pyrazolo[3,4-*b*]pyridines with different substituted groups, 3-amino-1*H*-pyrazol-5-ol **3b** was selected. To our delight, the reactions of **1** with **2a** and **3b** under identical conditions afforded the desired cyclopenta[*d*]pyrazolo [3,4-*b*]pyridin-1-ol **4i**–**k** in 70–88% yield (Table 2, entries 9–12). Similarly, the reaction of **1** with cyclohexanone **2b** or tetrahydrothiopyran-4-one **2c** and **3** also gave a satisfactory result and pyrazolo[3,4-*b*]pyridines **4** were obtained in 78–90% yield. The structure of **4n** was further confirmed by single crystal X-ray (Fig. 3). It is worth noting that this multi-component reaction smoothly proceeds to generate the desired products of type **III** with high yields in HOAc, avoiding the use of TFA (Scheme 3).

Table 1
Reaction of **1a** with **2a** and **3a** under different conditions

Entry	*T* (°C)	Time (min)	Yield[a] (%)
1	80	15	40
2	100	15	55
3	120	15	79
4	130	15	77
5	140	15	75

[a] Isolated yield.

Next, with the aim to improve the yields of **5a** in Scheme 2, we increased the amount of aldehydes and decreased that of cyclic ketones simultaneously to the feed ratio of **1a**/**2a**/**3a** in 2:1:1. After several trials, we found that the reaction in acidic condition resulted in main product **5**, but the products **4** as by-products were still isolated. So we attempted to change the reaction condition to basic condition. The reaction of **1a** and cyclopentanone **2a** with **3a** was initially investigated using various bases, such as K_2CO_3, Et_3N,

Table 2
The three-component synthesis of compounds **4**

Entry	Product[a]	Ar	2	3	Time (min)	Yield[b] (%)
1	**4a**	4-Chlorophenyl (**1a**)	**2a**	**3a**	15	79
2	**4b**	3,4-Dichlorophenyl (**1b**)	**2a**	**3a**	15	87
3	**4c**	4-Fluorophenyl (**1c**)	**2a**	**3a**	14	85
4	**4d**	4-Bromophenyl (**1d**)	**2a**	**3a**	15	84
5	**4e**	4-Tolyl (**1e**)	**2a**	**3a**	13	81
6	**4f**	4-Methoxyphenyl (**1f**)	**2a**	**3a**	15	80
7	**4g**	3,4,5-Trimethoxyphenyl (**1g**)	**2a**	**3a**	16	81
8	**4h**	Thien-2-yl (**1h**)	**2a**	**3a**	14	80
9	**4i**	4-Chlorophenyl (**1a**)	**2a**	**3b**	16	86
10	**4j**	4-Bromophenyl (**1c**)	**2a**	**3b**	15	88
11	**4k**	4-Tolyl (**1e**)	**2a**	**3b**	14	85
12	**4l**	4-Chlorophenyl (**1a**)	**2b**	**3b**	14	85
13	**4m**	4-Methoxyphenyl (**1f**)	**2b**	**3b**	15	90
14	**4n**	Thien-2-yl (**1h**)	**2b**	**3b**	14	87
15	**4o**	4-Chlorophenyl (**1a**)	**2c**	**3a**	15	89
16	**4p**	2,4-Dichlorophenyl (**1i**)	**2c**	**3a**	17	82
17	**4q**	4-Fluorophenyl (**1j**)	**2c**	**3a**	14	80
18	**4r**	4-Bromophenyl (**1b**)	**2c**	**3a**	13	84
19	**4s**	4-Nitrophenyl (**1k**)	**2c**	**3a**	15	85
20	**4t**	4-Hydroxy-3-nitrophenyl (**1l**)	**2c**	**3a**	15	82
21	**4u**	4-Tolyl (**1e**)	**2c**	**3a**	15	88
22	**4v**	4-Methoxyphenyl (**1f**)	**2c**	**3a**	16	80
23	**4w**	2,3-Dimethoxyphenyl (**1m**)	**2c**	**3a**	16	81
24	**4x**	3,4,5-Trimethoxyphenyl (**1g**)	**2c**	**3a**	18	79
25	**4y**	4-Hydroxy-3-methoxyphenyl (**1n**)	**2c**	**3a**	18	79
26	**4z**	Thien-2-yl (**1h**)	**2c**	**3a**	14	83
27	**4aa**	4-Bromophenyl (**1b**)	**2c**	**3b**	13	80
28	**4bb**	4-Tolyl (**1e**)	**2c**	**3b**	12	78
29	**4cc**	4-Methoxyphenyl (**1f**)	**2c**	**3b**	16	88
30	**4dd**	3,4-Dimethoxyphenyl (**1o**)	**2c**	**3b**	16	86
31	**4ee**	3,4,5-Trimethoxyphenyl (**1g**)	**2c**	**3b**	14	82
32	**4ff**	4-Dimethylaminophenyl (**1p**)	**2c**	**3b**	15	87
33	**4gg**	Thien-2-yl (**1h**)	**2c**	**3b**	13	80

[a] Reagents and conditions: HOAc (2.0 mL), 120 °C, MW.
[b] Isolated yield.

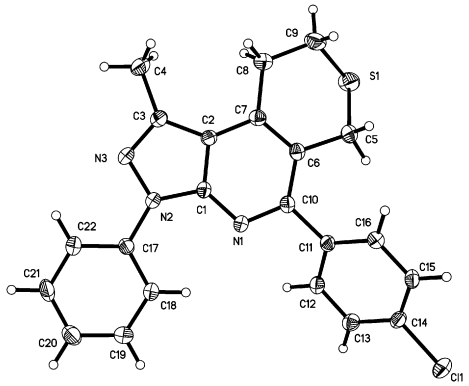
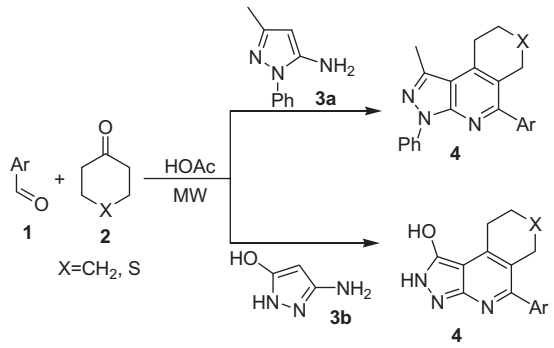
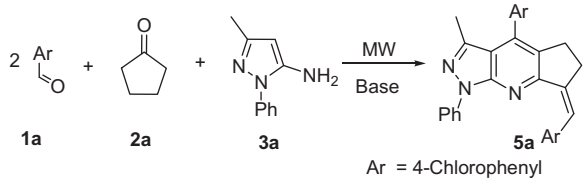


Fig. 3. ORTEP drawing of **4n**.[21]

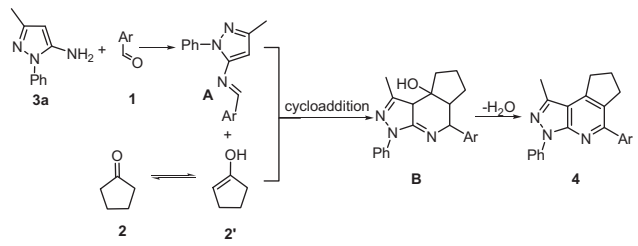


Scheme 3. Different reaction pathways for the condensation of 5-aminopyrazoles, aldehydes, and cyclic ketones.

piperidine, pyrrolidine, and *N*,*N*-dimethyl-4-aminopyridine (DMAP) under microwave (MW) irradiation. Although product **5** can be generated in the presence of all these bases (Scheme 5), the reaction also generated the intermediate **C**. When 0.2 equiv of NaOH was used as a base catalyst, the reaction in DMF resulted in product **5a** as a sole product in high yield (Table 3, entry 1) (Scheme 4). Under the optimized conditions mentioned above, the scope of this new MCR process was next examined using various readily available starting materials. As revealed in Table 3, a range of invaluable pyrazolopyridine derivatives can be synthesized in good to excellent yields. The results indicated that aromatic aldehydes bearing either electron donating or electron withdrawing functional groups, such as nitro, chloro, or methoxy were suitable for the synthesis of compounds **5**.



Scheme 4. Different reaction pathways for the condensation of 5-aminopyrazoles, aldehydes, and cyclic ketones.



Scheme 5. Proposed mechanism for products **4**.

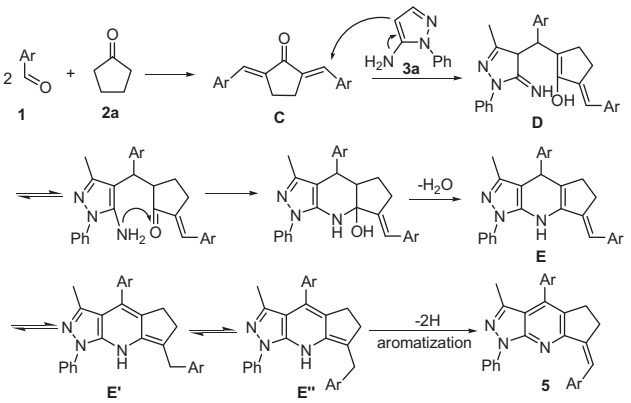
Table 3
The three-component synthesis of compounds **5**

Entry	Product[a]	Ar	2	3	Time (min)	Yield[b] (%)
1	**5a**	4-Chlorophenyl (**1a**)	**2a**	**3a**	15	86
2	**5b**	3,4-Dichlorophenyl (**1b**)	**2a**	**3a**	15	87
3	**5c**	4-Tolyl (**1e**)	**2a**	**3a**	14	80
4	**5d**	4-Methoxyphenyl (**1f**)	**2a**	**3a**	16	81
5	**5e**	3,4,5-Trimethoxyphenyl (**1g**)	**2a**	**3a**	17	78
6	**5f**	4-Chlorophenyl (**1a**)	**2a**	**3b**	17	78
7	**5g**	4-Bromophenyl (**1b**)	**2a**	**3b**	14	80
8	**5h**	4-Tolyl (**1e**)	**2a**	**3b**	14	75
9	**5i**	4-Methoxyphenyl (**1f**)	**2a**	**3b**	15	82
10	**5j**	4-Chlorophenyl (**1a**)	**2b**	**3b**	16	82
11	**5k**	Thien-2-yl (**1h**)	**2b**	**3b**	17	78

[a] Reagents and conditions: NaOH (0.2 equiv), 120 °C, DMF, MW.
[b] Isolated yield.

Using cyclic diketones the formation of pyrazolo[3,4-*b*]pyridines **I** involving Knoevenagel-type condensation, intermolecular Michael addition, and intramolecular cyclization has been reported.[18] Compared with type **I**, the formation of pyrazolo[3,4-*b*]pyridines **III** with cyclic monoketones and different aryl substituted patterns should undergo another reaction process. Based on analyses of literatures and experimental results, we reasoned that the reaction underwent [4+2] cycloaddition process. This type of [4+2] cycloaddition was well precedented.[18] Therefore, a reasonable mechanism for type **III** is proposed in Scheme 5. Presumably, in the

presence of HOAc, cycloketone **2** is in equilibrium with the enol form **2′**. The condensed intermediate **A** undergoes a [4+2] cycloaddition with the enol form **2′** to form intermediate **B**. The subsequent dehydration of **B** and aromatization results in **4**. This reaction type is similar to Povarov reaction.[19] The latter underwent sequence of Knoevenagel-type condensation (**2** to **C**), intermolecular Michael addition (**C** to **D**), intramolecular cyclization (**D** to **E** to **E″**) and dehydration (**E″** to **5**), which is similar to the formation of pyrazolo[3,4-*b*]pyridines **I** (Scheme 6).



Scheme 6. Proposed mechanism for products **5**.

3. Conclusion

We have described microwave-assisted three-component heterocyclization reactions (aminopyrazole, cycloketones, and aldehydes) as an alternative method for divergent synthesis of pyrazolopyridine derivatives with different substituted patterns by controlling the reaction condition. The reaction under acidic condition proceeds by selective [4+2] heterocyclization obtaining pyrazolo[3,4-*b*]pyridines **4** in good yields, showing that the synthetic route allows us to build blocks of fused pyrazolo[3,4-*b*]pyridine derivatives with a wide diversity of substituents. The base condition gave the different substituted patterns on the fused pyrazolopyridine framework **5**. This methodology is simple, practical and is a regioselective alternative synthetic route to obtain good yields of pyrazolopyridine derivatives by microwave irradiation. This method is much more efficient due to short reaction times and easy work-up.

4. Experimental section

4.1. General

Microwave irradiation was carried out with Initiator from Biotage Company, Sweden. Melting points were determined in open capillaries and were uncorrected. IR spectra were taken on an FT-IR-Tensor 27 spectrometer in KBr pellets and reported in cm^{-1}. ^1H NMR spectra were measured on a Bruker DPX 400 MHz spectrometer in DMSO-d_6 with chemical shift (δ) given in parts per million relative to TMS as internal standard. HRMS (ESI) was determined by using microTOF-Q II HRMS/MS instrument (Bruker). X-ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

4.2. Typical procedure for the preparation of 5-(4-chlorophenyl)-1-methyl-3-phenyl-3,6,7,8-tetrahydrocyclopenta[*d*]pyrazolo[3,4-*b*]pyridine (4a)

In a 10-mL reaction vial, the 4-chlorobenzaldehyde (0.14 g, 1 mmol), cyclopentanone (0.13 g, 1.5 mmol), 3-methyl-1-phenyl-1*H*-pyrazol-5-amine (0.17 g, 1 mmol), and HOAc (2.0 mL) were mixed and stirred at room temperature for 3 min. Then the mixture was heated for 15 min at 120 °C under microwave irradiation. The automatic mode stirring helped the mixing and uniform heating of the reactants. Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature and then diluted with cold water (40 mL). The solid product was collected by Büchner filtration and was purified by recrystallization from 95% EtOH to afford the desired pure products **4a** as pale yellow solid.

Pale yellow solid, mp: 150–152 °C. IR (KBr, ν, cm^{-1}): 3000, 2768, 1598, 1506, 758. ^1H NMR ($CDCl_3$, 400 MHz) (δ, ppm): 8.38 (d, J=8.0 Hz, 2H, ArH), 7.84 (d, J=8.4 Hz, 2H, ArH), 7.49–7.46 (m, 4H, ArH), 7.26–7.22 (m, 1H, ArH), 3.34 (t, J=7.2 Hz, 2H, CH_2), 3.17 (t, J=7.2 Hz, 2H, CH_2), 2.72 (s, 3H, CH_3), 2.29–2.21 (m, 2H, CH_2). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 152.6, 150.8, 149.3, 141.9, 140.1, 138.9, 134.6, 130.3, 128.9, 128.5, 124.9, 120.8, 120.3, 113.9, 32.6, 31.6, 25.7, 14.0. HRMS (ESI): m/z calcd for: $C_{22}H_{18}ClN_3Na$, 382.1082, found: 382.1086.

4.2.1. 5-(3,4-Dichlorophenyl)-1-methyl-3-phenyl-3,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridine ***4b***. Pale yellow solid, mp: 151–152 °C. IR (KBr, ν, cm^{-1}): 3068, 2961, 1598, 1506, 1409, 1308, 1230, 855, 751, 711, 691. ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.34 (d, J=8.0 Hz, 2H, ArH), 7.96 (d, J=1.6 Hz, 1H, ArH), 7.72 (dd, J_1=2.0 Hz, J_2=8.0 Hz, 1H, ArH), 7.56–7.50 (m, 3H, ArH), 7.25–7.23 (m, 1H, ArH), 3.32 (t, J=7.6 Hz, 2H, CH_2), 3.15 (t, J=7.2 Hz, 2H, CH_2), 2.71 (s, 3H, CH_3), 2.29–2.21 (m, 2H, CH_2). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 151.3, 150.7, 149.6, 141.9, 140.4, 140.0, 132.7, 132.5, 130.8, 130.8, 130.2, 129.0, 129.0, 128.2, 125.1, 120.9, 120.4, 114.1, 32.5, 31.6, 25.7, 14.1. HRMS (ESI): m/z calcd for: $C_{22}H_{18}Cl_2N_3$, 394.0873, found: 394.0883.

4.2.2. 5-(4-Fluorophenyl)-1-methyl-3-phenyl-3,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridine ***4c***. Pale yellow solid, mp: 109–110 °C. IR (KBr, ν, cm^{-1}): 2966, 2788, 1597, 1508, 1237, 1158, 837, 755. ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.38 (d, J=7.6 Hz, 2H, ArH), 7.89 (dd, J_1=5.6 Hz, J_2=8.8 Hz, 1H, ArH), 7.58–7.47 (m, 3H, ArH), 7.24–7.09 (m, 3H, ArH), 3.34 (t, J=7.6 Hz, 2H, CH_2), 3.17 (t, J=7.2 Hz, 2H, CH_2), 2.72 (s, 3H, CH_3), 2.29–2.21 (m, 2H, CH_2). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 162.3 ($^1J_{CF}$=222.7), 150.8, 149.2, 141.9, 140.1, 130.8 ($^3J_{CF}$=8.4 Hz), 130.7, 130.5 ($^{3'}J_{CF}$=8.4 Hz), 128.9, 124.9, 123.4 ($^4J_{CF}$=1.9 Hz), 120.9, 120.4, 115.5 ($^2J_{CF}$=21.0 Hz), 115.2 ($^{2'}J_{CF}$=21.3 Hz), 113.8, 31.6, 29.3, 25.8, 14.1. HRMS (ESI): m/z calcd for: $C_{22}H_{18}FN_3Na$, 366.1377, found: 366.1390.

4.2.3. 5-(4-Bromophenyl)-1-methyl-3-phenyl-3,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridine ***4d***. Pale yellow solid, mp: 135–136 °C. IR (KBr, ν, cm^{-1}): 2950, 1594, 1506, 1488, 1308, 1008, 834, 753, 691. ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.37 (d, J=7.6 Hz, 2H, ArH), 7.76 (d, J=8.4 Hz, 2H, ArH), 7.62 (d, J=8.4 Hz, 2H, ArH), 7.50–7.46 (m, 2H, ArH), 7.25–7.22 (m, 1H, ArH), 3.33 (t, J=7.2 Hz, 2H, CH_2), 3.15 (t, J=7.6 Hz, 2H, CH_2), 2.71 (s, 3H, CH_3), 2.28–2.20 (m, 2H, CH_2). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 152.7, 150.8, 149.3, 141.9, 140.1, 139.4, 131.4, 130.6, 128.9, 125.0, 123.0, 120.9, 120.4, 113.9, 32.5, 31.6, 25.7, 14.0. HRMS (ESI): m/z calcd for: $C_{22}H_{19}BrN_3$, 404.0757, found: 404.0782.

4.2.4. 1-Methyl-3-phenyl-5-(p-tolyl)-3,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridine ***4e***. Pale yellow solid, mp: 130–132 °C. IR (KBr, ν, cm^{-1}): 2962, 2920, 1596, 1506, 1409, 1359, 1308, 1255, 1180, 1129, 758, 685, 649. ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.42 (d, J=8.4 Hz, 2H, ArH), 7.80 (d, J=8.0 Hz, 2H, ArH), 7.47 (t, J=8.0 Hz, 2H, ArH), 7.31–7.28 (m, 3H, ArH), 3.31 (t, J=7.6 Hz, 2H, CH_2), 3.18 (t, J=7.2 Hz, 2H, CH_2), 2.70 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.25–2.18 (m, 2H, CH_2). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 154.1, 151.0, 148.8, 140.2, 138.5, 137.8, 130.8, 129.3, 128.9, 128.6, 124.8, 120.8, 120.4,

113.6, 32.7, 31.6, 25.8, 21.4, 14.1. HRMS (ESI): *m*/*z* calcd for: $C_{23}H_{22}N_3$, 340.1809, found: 340.1827.

4.2.5. 5-(4-Methoxyphenyl)-1-methyl-3-phenyl-3,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridine ***4f***. Pale yellow solid, mp: 109–110 °C. IR (KBr, *ν*, cm^{-1}): 2931, 1596, 1507, 1409, 1254, 1176, 1037, 829, 755, 648. ^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 8.41 (d, *J*=7.6 Hz, 2H, ArH), 7.88 (d, *J*=8.8 Hz, 2H, ArH), 7.49 (d, *J*=8.0 Hz, 2H, ArH), 7.22 (d, *J*=7.6 Hz, 1H, ArH), 7.03 (d, *J*=8.8 Hz, 2H, ArH), 3.88 (s, 3H, OCH_3), 3.32 (t, *J*=7.2 Hz, 2H, CH_2), 3.19 (t, *J*=7.2 Hz, 2H, CH_2), 2.71 (s, 3H, CH_3), 2.27–2.20 (m, 2H, CH_2). ^{13}C NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 160.0, 151.0, 148.9, 141.8, 140.2, 133.2, 130.7, 130.4, 130.0, 128.9, 124.8, 120.8, 120.4, 113.7, 55.4, 32.8, 31.6, 25.8, 14.1. HRMS (ESI): *m*/*z* calcd for: $C_{23}H_{22}N_3O$, 356.1758, found: 356.1763.

4.2.6. 1-Methyl-3-phenyl-5-(3,4,5-trimethoxyphenyl)-3,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridine ***4g***. Yellow solid, mp: 167–168 °C. IR (KBr, *ν*, cm^{-1}): 2940, 2839, 1597, 1506, 1463, 1407, 1363, 1235, 1119, 1006, 753, 687. ^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 8.43 (d, *J*=8.4 Hz, 2H, ArH), 7.48 (t, *J*=8.0 Hz, 2H, ArH), 7.23 (t, *J*=7.2 Hz, 1H, ArH), 7.18 (s, 2H, ArH), 3.95 (s, 6H, OCH_3), 3.93 (s, 3H, OCH_3), 3.33 (t, *J*=7.2 Hz, 2H, CH_2), 3.22 (t, *J*=7.2 Hz, 2H, CH_2), 2.71 (s, 3H, CH_3), 2.29–2.17 (m, 2H, CH_2). ^{13}C NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 153.5, 153.0, 150.8, 149.2, 141.9, 140.2, 138.8, 136.0, 130.6, 128.9, 124.9, 120.3, 113.7, 106.6, 61.0, 56.3, 32.9, 31.6, 25.8, 14.1. HRMS (ESI): *m*/*z* calcd for: $C_{25}H_{26}N_3O_3$, 416.1969, found: 416.1972.

4.2.7. 5-(Thiophene-2-yl)-1-methyl-3-phenyl-3,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridine ***4h***. Yellow solid, mp: 170–172 °C. IR (KBr, *ν*, cm^{-1}): 3066, 2971, 2849, 1594, 1504, 1463, 1410, 1381, 1135, 1027, 858, 755, 692. ^1H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 8.45 (d, *J*=7.6 Hz, 2H, ArH), 7.57 (d, *J*=3.2 Hz, 1H, thienyl–H), 7.51 (t, *J*=7.6 Hz, 2H, ArH), 7.44 (d, *J*=4.8 Hz, 1H, thienyl–H), 7.23 (d, *J*=7.2 Hz, 1H, ArH), 7.14 (t, *J*=4.0 Hz, 1H, thienyl–H), 3.24 (t, *J*=7.2 Hz, 2H, CH_2), 3.19 (t, *J*=7.2 Hz, 2H, CH_2), 2.62 (s, 3H, CH_3), 2.30–2.23 (m, 2H, CH_2). ^{13}C NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 150.1, 149.3, 147.6, 146.2, 142.0, 140.2, 128.9, 128.8, 128.2, 128.0, 127.1, 124.7, 120.0, 113.7, 32.5, 31.3, 24.8, 14.0. HRMS (ESI): *m*/*z* calcd for: $C_{20}H_{18}N_3S$, 332.1216, found: 332.1217.

4.2.8. 5-(4-Chlorophenyl)-2,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridin-1-ol ***4i***. Yellow solid, mp: 281–283 °C. IR (KBr, *ν*, cm^{-1}): 3417, 3417, 2950, 2842, 1592, 1261, 1206, 1091, 1015, 828. ^1H NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 11.88 (s, 1H, NH), 7.52 (s, 4H, ArH), 2.97 (t, *J*=7.6 Hz, 2H, CH_2), 2.83 (t, *J*=7.2 Hz, 2H, CH_2), 2.06–2.02 (m, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 167.5, 134.0, 132.9, 131.5, 131.4, 130.6, 128.6, 127.8, 127.7, 126.9, 34.1, 28.9, 23.6. HRMS (ESI): *m*/*z* calcd for: $C_{15}H_{13}ClN_3O$, 286.0742, found: 286.0741.

4.2.9. 5-(4-Bromophenyl)-2,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridin-1-ol ***4j***. Yellow solid, mp: >300 °C. IR (KBr, *ν*, cm^{-1}): 3215, 2946, 1594, 1541, 1262, 1206, 1009, 825, 669. ^1H NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 11.88 (s, 1H, NH), 10.59 (s, 1H, OH), 7.66 (d, *J*=8.0 Hz, 2H, ArH), 7.46 (d, *J*=8.0 Hz, 2H, ArH), 2.97 (t, *J*=7.2 Hz, 2H, CH_2), 2.83 (t, *J*=6.8 Hz, 2H, CH_2), 2.09–2.03 (m, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 167.6, 154.0, 143.6, 134.4, 131.7, 130.6, 126.9, 121.6, 112.7, 99.9, 34.1, 28.9, 23.6. HRMS (ESI): *m*/*z* calcd for: $C_{15}H_{13}BrN_3O$, 330.0237, found: 330.0238.

4.2.10. 5-(p-Tolyl)-2,6,7,8-tetrahydrocyclopenta[d]pyrazolo[3,4-b]pyridin-1-ol ***4k***. Brown solid, mp: >300 °C. IR (KBr, *ν*, cm^{-1}): 3415, 3055, 2939, 2839, 1595, 1541, 1522, 1395, 1265, 1220, 1205, 824. ^1H NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 11.79 (s, 1H, NH), 10.58 (s, 1H, OH), 7.39 (d, *J*=8.0 Hz, 2H, ArH), 7.26 (d, *J*=7.6 Hz, 2H, ArH), 2.95 (t, *J*=7.2 Hz, 2H, CH_2), 2.83 (t, *J*=6.8 Hz, 2H, CH_2), 2.37 (s, 3H, CH_3), 2.06–2.01 (m, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 167.3, 154.1, 139.8, 137.4, 132.3, 129.5, 128.2, 126.8, 112.7, 100.2, 34.1, 29.2, 23.6, 20.9. HRMS (ESI): *m*/*z* calcd for: $C_{16}H_{16}N_3O$, 266.1288, found: 266.1287.

4.2.11. 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-3H-pyrazolo[3,4-c]isoquinolin-1-ol ***4l***. White solid, mp: >300 °C. IR (KBr, *ν*, cm^{-1}): 3526, 3442, 3046, 2938, 1599, 1541, 1495, 1404, 1346, 1271, 1168, 1017, 911, 827, 798. ^1H NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 11.08 (s, 1H, NH), 7.50 (d, *J*=8.4 Hz, 2H, ArH), 7.34 (d, *J*=8.4 Hz, 2H, ArH), 2.93 (t, *J*=6.4 Hz, 2H, CH_2), 2.49 (t, *J*=6.4 Hz, 2H, CH_2), 1.84–1.78 (m, 2H, CH_2), 1.68–1.62 (m, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 158.6, 154.8, 152.1, 142.4, 134.3, 132.5, 131.0, 127.7, 121.4, 101.8, 33.4, 26.2, 22.7, 22.3. HRMS (ESI): *m*/*z* calcd for: $C_{16}H_{13}ClN_3O$, 298.0741, found: 298.0771.

4.2.12. 5-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-3H-pyrazolo[3,4-c]isoquinolin-1-ol ***4m***. Pale yellow solid, mp: >300 °C. IR (KBr, *ν*, cm^{-1}): 3546, 3446, 3046, 2933, 2836, 1591, 1510, 1250, 1176, 1031, 825, 585. ^1H NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 10.98 (s, 1H, NH), 7.24 (d, *J*=8.8 Hz, 2H, ArH), 6.98 (d, *J*=8.8 Hz, 2H, ArH), 3.81 (s, 3H, OCH_3), 2.91 (t, *J*=6.4 Hz, 2H, CH_2), 2.51 (t, *J*=6.4 Hz, 2H, CH_2), 1.82–1.76 (m, 2H, CH_2), 1.65–1.60 (m, 2H, CH_2). ^{13}C NMR (DMSO-d_6, 400 MHz) (*δ*, ppm): 158.7, 158.5, 155.1, 152.4, 143.8, 130.5, 127.4, 121.7, 113.0, 102.2, 55.0, 33.4, 26.4, 22.8, 22.3. HRMS (ESI): *m*/*z* calcd for: $C_{17}H_{16}N_3O_2$, 294.1237, found: 294.1250.

4.2.13. 5-(Thiophene-2-yl)-6,7,8,9-tetrahydro-3H-pyrazolo[3,4-c]isoquinolin-1-ol ***4n***. Yellow solid, mp: >300 °C. IR (KBr, *ν*, cm^{-1}): 3479, 3415, 3207, 2953, 2867, 1673, 1617, 1541, 1428, 1202, 1138, 1060, 728. ^1H NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 11.91 (s, 1H, NH), 7.75–7.74 (q, 1H, hienyl–H), 7.20–7.18 (m, 2H, thienyl–H), 2.95 (t, *J*=6.4 Hz, 2H, CH_2), 2.66 (t, *J*=6.0 Hz, 2H, CH_2), 1.85–1.79 (m, 2H, CH_2), 1.72–1.67 (m, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 157.5, 154.4, 150.1, 138.2, 134.2, 129.4, 127.6, 126.9, 122.8, 103.0, 32.6, 26.6, 22.6, 21.9. HRMS (ESI): *m*/*z* calcd for: $C_{14}H_{13}N_3NaOS$, 294.0672, found: 294.0672.

4.2.14. 5-(4-Chlorophenyl)-1-methyl-3-phenyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4o***. Gray yellow solid, mp: 200–202 °C. IR (KBr, *ν*, cm^{-1}): 3068, 2963, 2896, 1592, 1577, 1506, 1415, 1383, 1286, 1104, 1090, 1014, 911, 8839, 756, 693. ^1H NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 8.25–8.23 (m, 2H, ArH), 7.63–7.61 (m, 4H, ArH), 7.50 (s, 2H, ArH), 7.27 (s, 1H, ArH), 3.78 (s, 2H, CH_2), 3.61–3.54 (m, 2H, CH_2), 3.06–3.00 (m, 2H, CH_2), 2.76 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 156.7, 149.3, 142.3, 141.9, 139.6, 138.6, 134.7, 130.8, 129.0, 128.6, 125.3, 122.6, 120.6, 115.0, 113.2, 27.9, 27.7, 25.6, 16.1. HRMS (ESI): *m*/*z* calcd for: $C_{22}H_{19}ClN_3S$, 392.0982, found: 392.0982.

4.2.15. 5-(2,4-Dichlorophenyl)-1-methyl-3-phenyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4p***. White solid, mp: 206–207 °C. IR (KBr, *ν*, cm^{-1}): 3067, 2890, 1593, 1575, 1505, 1488, 1408, 1383, 1288, 1238, 1116, 1099, 829, 757, 682, 637. ^1H NMR (400 MHz, DMSO-d_6) (*δ*, ppm): 8.16 (d, *J*=7.2 Hz, 2H, ArH), 7.82 (s, 1H, ArH), 7.61–7.49 (m, 4H, ArH), 7.26 (t, *J*=6.8 Hz, 1H, ArH), 3.36 (s, 2H, CH_2), 3.51–3.48 (m, 2H, CH_2), 3.02–3.00 (m, 2H, CH_2), 2.76 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 154.8, 149.1, 141.7, 139.5, 137.7, 135.0, 133.9, 131.6, 129.5, 129.0, 127.4, 125.4, 122.8, 120.8, 115.6, 113.2, 27.9, 26.8, 25.3, 16.1. HRMS (ESI): *m*/*z* calcd for: $C_{22}H_{18}Cl_2N_3S$, 426.0593, found: 426.0565.

4.2.16. 5-(4-Fluorophenyl)-1-methyl-3-phenyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4q***. Bright yellow solid, mp: 174–176 °C. IR (KBr, *ν*, cm^{-1}): 3067, 3041, 2923, 2898,

1595, 1567, 1508, 1491, 1412, 1387, 1357, 1220, 1157, 1143, 1104, 1014, 839, 764, 694, 645. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.23 (d, J=8.0 Hz, 2H, ArH), 7.67–7.63 (m, 2H, ArH), 7.51 (t, J=8.0 Hz, 2H, ArH), 7.36 (t, J=8.8 Hz, 2H, ArH), 7.27 (t, J=7.2 Hz, 1H, ArH), 3.76 (s, 2H, CH_2), 3.59–3.56 (m, 2H, CH_2), 3.01 (t, J=6.0 Hz, 2H, CH_2), 2.74 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 162.9 ($^1J_{CF}$=246.4), 156.9, 149.3, 142.2, 141.9, 139.6, 136.2 ($^4J_{CF}$=3.2 Hz), 131.2 ($^3J_{CF}$=8.2 Hz), 129.0, 125.3, 122.6, 120.6, 115.3 ($^2J_{CF}$=21.4 Hz), 114.9, 113.2, 27.9, 27.7, 25.6, 16.1. HRMS (ESI): m/z calcd for: $C_{22}H_{19}FN_3S$, 376.1278, found: 376.1278.

4.2.17. 5-(4-Bromophenyl)-1-methyl-3-phenyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4r***. White solid, mp: 206–207 °C. IR (KBr, ν, cm^{-1}): 2996, 2888, 1588, 1576, 1506, 1489, 1417, 1382, 1103, 1009, 836, 756, 693. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.24 (d, J=8.0 Hz, 2H, ArH), 7.74 (d, J=7.6 Hz, 2H, ArH), 7.57 (d, J=7.6 Hz, 2H, ArH), 7.51 (t, J=7.6 Hz, 2H, ArH), 7.27 (t, J=7.6 Hz, 1H, ArH), 3.78 (s, 2H, CH_2), 3.58 (m, 2H, CH_2), 3.03 (m, 2H, CH_2), 2.76 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 156.7, 149.3, 142.4, 141.9, 139.6, 139.1, 131.5, 131.1, 131.0, 129.0, 125.3, 122.9, 122.5, 120.6, 115.0, 27.9, 27.7, 25.6, 16.1. HRMS (ESI): m/z calcd for: $C_{22}H_{19}BrN_3S$, 436.0477, found: 436.0465.

4.2.18. 1-Methyl-5-(4-nitrophenyl)-3-phenyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4s***. Yellow solid, mp: 206–207 °C. IR (KBr, ν, cm^{-1}): 3070, 2900, 1597, 1569, 1523, 1507, 1438, 1417, 1348, 757. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.37 (d, J=8.4 Hz, 2H, ArH), 8.23 (d, J=8.0 Hz, 2H, ArH), 7.90 (d, J=8.4 Hz, 2H, ArH), 7.51 (t, J=7.6 Hz, 2H, ArH), 7.27 (t, J=7.2 Hz, 1H, ArH), 3.79 (s, 2H, CH_2), 3.61 (t, J=6.0 Hz, 2H, CH_2), 3.04 (t, J=6.0 Hz, 2H, CH_2), 2.78 (s, 3H, CH_3). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 155.2, 148.4, 147.4, 146.1, 143.6, 142.6, 139.0, 131.9, 130.7, 129.1, 125.3, 123.5, 122.8, 120.0, 115.2, 112.7, 27.2, 27.0, 24.5, 15.6. HRMS (ESI): m/z calcd for: $C_{22}H_{19}N_4O_2S$, 403.1223, found: 403.1217.

4.2.19. 4-(1-Methyl-3-phenyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridin-5-yl)-2-nitrophenol ***4t***. Yellow solid, mp: 199–200 °C. IR (KBr, ν, cm^{-1}): 3243, 3076, 2930, 2899, 1630, 1582, 1539, 1509, 1417, 1356, 1320, 1289, 1178, 837, 756, 691, 649. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.38 (s, 1H, OH), 8.24 (d, J=8.0 Hz, 2H, ArH), 8.10 (d, J=2.0 Hz, 1H, ArH), 7.80 (dd, J_1=2.0 Hz, J_2=8.4 Hz, 1H, ArH), 7.51 (t, J=7.6 Hz, 2H, ArH), 7.28–7.25 (m, 2H, ArH), 3.82 (s, 2H, CH_2), 3.56 (t, J=6.0 Hz, 2H, CH_2), 3.01 (t, J=6.0 Hz, 2H, CH_2), 2.74 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 155.1, 154.7, 149.2, 142.7, 142.0, 139.5, 138.6, 133.2, 132.6, 129.1, 125.9, 125.5, 122.4, 120.5, 120.1, 115.2, 28.0, 27.7, 25.5, 16.1. HRMS (ESI): m/z calcd for: $C_{22}H_{19}N_4O_3S$, 419.1172, found: 419.1171.

4.2.20. 1-Methyl-3-phenyl-5-p-tolyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4u***. Gray solid, mp: 198–199 °C. IR (KBr, ν, cm^{-1}): 3067, 2920, 1595, 1567, 1506, 1415, 1383, 1353, 1275, 1141, 1018, 829, 759, 695, 684. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.26 (d, J=8.0 Hz, 2H, ArH), 7.49 (d, J=8.0 Hz, 4H, ArH), 7.35 (d, J=7.6 Hz, 2H, ArH), 7.26 (d, J=7.6 Hz, 1H, ArH), 3.78 (s, 2H, CH_2), 3.57 (t, J=6.4 Hz, 2H, CH_2), 3.03 (t, J=6.0 Hz, 2H, CH_2), 2.76 (s, 3H, CH_3), 2.41 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 158.1, 149.4, 141.9, 141.8, 139.8, 138.4, 137.4, 129.3, 129.0, 128.9, 125.1, 122.7, 120.6, 114.7, 28.0, 27.8, 25.6, 21.4, 16.1. HRMS (ESI): m/z calcd for: $C_{23}H_{22}N_3S$, 372.1529, found: 372.1526.

4.2.21. 5-(4-Methoxyphenyl)-1-methyl-3-phenyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4v***. White solid, mp: 164–165 °C. IR (KBr, ν, cm^{-1}): 2975, 2914, 2836, 1589, 1505, 1407, 1367, 1301, 1250, 1170, 1108, 1033, 836, 757, 680. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.27 (d, J=7.6 Hz, 2H, ArH), 7.56 (d, J=8.4 Hz, 2H, ArH), 7.50 (t, J=7.6 Hz, 2H, ArH), 7.25 (t, J=7.2 Hz, 1H, ArH), 7.08 (d, J=8.4 Hz, 2H, ArH), 3.84 (s, 3H, OCH_3), 3.80 (s, 2H, CH_2), 3.55 (t, J=6.0 Hz, 2H, CH_2), 3.01 (t, J=6.0 Hz, 2H, CH_2), 2.74 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 159.9, 157.7, 149.4, 142.0, 141.8, 139.8, 132.6, 130.8, 128.9, 125.1, 122.7, 120.6, 114.6, 113.7, 55.4, 28.1, 27.7, 25.7, 16.1. HRMS (ESI): m/z calcd for: $C_{23}H_{22}N_3OS$, 388.1478, found: 388.1476.

4.2.22. 5-(2,3-Dimethoxyphenyl)-1-methyl-3-phenyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4w***. White solid, mp: 200–202 °C. IR (KBr, ν, cm^{-1}): 3077, 2930, 2835, 1597, 1573, 1506, 1474, 1413, 1384, 1359, 1288, 1268, 1230, 1130, 1077, 1062, 1004, 757, 693. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.22 (d, J=8.0 Hz, 2H, ArH), 7.49 (t, J=8.0 Hz, 2H, ArH), 7.24 (t, J=7.2 Hz, 1H, ArH), 7.20–7.19 (m, 2H, ArH), 6.86–6.84 (m, 1H, ArH), 3.88 (s, 3H, OCH_3), 3.57 (t, J=6.0 Hz, 2H, CH_2), 3.54 (s, 3H, OCH_3), 3.50 (s, 2H, CH_2), 3.05–2.95 (m, 2H, CH_2), 2.75 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 155.9, 152.8, 149.2, 146.6, 141.9, 141.0, 139.8, 135.0, 128.9, 125.1, 124.3, 123.5, 122.3, 120.6, 115.2, 112.5, 61.4, 55.9, 27.9, 27.1, 25.4, 16.1. HRMS (ESI): m/z calcd for: $C_{24}H_{24}N_3O_2S$, 418.1584, found: 418.1569.

4.2.23. 1-Methyl-3-phenyl-5-(3,4,5-trimethoxyphenyl)-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4x***. White solid, mp: 230–231 °C. IR (KBr, ν, cm^{-1}): 2990, 2888, 1587, 1576, 1507, 1413, 1371, 1288, 1230, 1126, 1017, 751, 696. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.27 (d, J=8.0 Hz, 2H, ArH), 7.52 (d, J=7.6 Hz, 2H, ArH), 7.27 (t, J=7.2 Hz, 1H, ArH), 6.85 (s, 2H, ArH), 3.83 (s, 6H, OCH_3), 3.82–3.80 (m, 2H, CH_2), 3.74 (s, 3H, OCH_3), 3.58 (t, J=6.0 Hz, 2H, CH_2), 3.02 (t, J=6.0 Hz, 2H, CH_2), 2.76 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 157.7, 153.1, 149.2, 142.3, 141.9, 139.7, 138.5, 135.6, 129.0, 125.2, 122.6, 120.6, 114.8, 106.7, 61.0, 56.3, 27.9, 27.7, 25.6, 16.1. HRMS (ESI): m/z calcd for: $C_{25}H_{26}N_3O_3S$, 448.1689, found: 448.1651.

4.2.24. 2-Methoxy-4-(1-methyl-3-phenyl-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridin-5-yl)phenol ***4y***. Gray white solid, mp: 193–194 °C. IR (KBr, ν, cm^{-1}): 3382, 3005, 2895, 2835, 1596, 1563, 1517, 1506, 1414, 1290, 1262, 1197, 1141, 1029, 819, 761, 693. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 9.38 (s, 1H, OH), 8.29 (d, J=8.0 Hz, 2H, ArH), 7.51 (t, J=8.0 Hz, 2H, ArH), 7.26 (t, J=7.2 Hz, 1H, ArH), 7.16 (s, 1H, ArH), 7.04–7.01 (m, 1H, ArH), 6.90 (d, J=8.0 Hz, 1H, ArH), 3.84 (s, 2H, CH_2), 3.83 (s, 2H, OCH_3), 3.55 (t, J=6.0 Hz, 2H, CH_2), 3.02 (t, J=6.0 Hz, 2H, CH_2), 2.74 (s, 3H, CH_3). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 157.6, 148.6147.2, 147.2, 142.7, 142.3, 139.3, 130.8, 129.0, 125.0, 122.9, 122.1, 119.7, 115.1, 114.2, 113.5, 68.5, 55.7, 30.7, 27.4, 27.2, 24.7, 15.6. HRMS (ESI): m/z calcd for: $C_{23}H_{22}N_3O_2S$, 404.1427, found: 404.1388.

4.2.25. 1-Methyl-3-phenyl-5-(thiophen-2-yl)-3,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridine ***4z***. Gray yellow solid, mp: 164–165 °C. IR (KBr, ν, cm^{-1}): 3067, 2893, 1600, 1568, 1506, 1442, 1416, 1384, 1358, 1291, 1237, 1137, 751, 708, 695. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.33 (d, J=8.0 Hz, 2H, ArH), 7.79 (d, J=4.8 Hz, 1H, ArH), 7.62 (d, J=3.6 Hz, 1H, thienyl–H), 7.54 (t, J=7.6 Hz, 2H, ArH), 7.28 (t, J=3.6 Hz, 1H, thienyl–H), 7.23 (t, J=4.0 Hz, 1H, thienyl–H), 4.10 (s, 2H, CH_2), 3.56 (t, J=6.0 Hz, 2H, CH_2), 3.01 (t, J=6.0 Hz, 2H, CH_2), 2.70 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 150.6, 148.8, 144.2, 142.2, 142.0, 139.6, 129.0, 128.4, 128.3, 127.5, 125.2, 121.6, 120.3, 114.9, 28.4, 28.3, 25.2, 16.1. HRMS (ESI): m/z calcd for: $C_{20}H_{18}N_3S_2$, 364.0936, found: 364.0960.

4.2.26. 5-(4-Bromophenyl)-2,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridin-1-ol ***4aa***. Pink solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3096, 2922, 1595, 1539, 1490, 1402, 1270, 1209, 1146, 1013, 829, 628. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.99 (s, 1H, NH),

7.68 (d, J=8.0 Hz, 2H, ArH), 7.30 (d, J=8.4 Hz, 2H, ArH), 3.58 (s, 2H, CH_2), 3.18 (t, J=6.4 Hz, 2H, CH_2), 2.94 (t, J=6.8 Hz, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 158.9, 154.5, 151.4, 140.1, 133.4, 131.7, 130.8, 121.5, 100.9, 33.8, 30.7, 24.9, 24.8. HRMS (ESI): m/z calcd for: $C_{15}H_{13}BrN_3OS$, 361.9958, found: 361.9943.

4.2.27. 5-p-Tolyl-2,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridin-1-ol ***4bb***. White solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3078, 2914, 1594, 1437, 1398, 1269, 1233, 1128, 1080, 831, 797. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.93 (s, 1H, NH), 10.57 (s, 1H, OH), 7.29 (d, J=7.6 Hz, 2H, ArH), 7.24 (d, J=8.0 Hz, 2H, ArH), 3.61 (s, 2H, CH_2), 3.18 (t, J=6.4 Hz, 2H, CH_2), 2.94 (t, J=6.4 Hz, 2H, CH_2), 2.39 (s, 3H, CH_3). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 163.9, 159.9, 156.8, 146.7, 142.7, 136.6, 134.8, 133.7, 126.9, 106.4, 39.1, 30.2, 30.1, 26.1. HRMS (ESI): m/z calcd for: $C_{16}H_{16}N_3OS$, 298.1009, found: 298.1006.

4.2.28. 5-(4-Methoxyphenyl)-2,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridin-1-ol ***4cc***. Pink solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3063, 2934, 2835, 1600, 1548, 1518, 1393, 1293, 1249, 1173, 1031, 832, 799, 592. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.90 (s, 1H, NH), 7.29 (d, J=8.4 Hz, 2H, ArH), 7.04 (d, J=8.8 Hz, 2H, ArH), 3.83 (s, 3H, OCH_3), 3.64 (s, 2H, CH_2), 3.18 (t, J=6.4 Hz, 2H, CH_2), 2.94 (t, J=6.4 Hz, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 159.1, 158.7, 141.3, 139.9, 131.1, 126.2, 122.4, 121.7, 113.3, 101.3, 55.1, 33.9, 24.9, 24.9. HRMS (ESI): m/z calcd for: $C_{16}H_{16}N_3O_2S$, 314.0958, found: 314.0970.

4.2.29. 5-(3,4-Dimethoxyphenyl)-2,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridin-1-ol ***4dd***. Brown solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3200, 2967, 1587, 1488, 1201, 1072, 1011, 833. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.94 (s, 1H, NH), 10.52 (s, 1H, OH), 7.06 (d, J=8.4 Hz, 1H, ArH), 6.96 (d, J=2.0 Hz, 1H, ArH), 6.89 (dd, J_1=2.0 Hz, J_2=8.0 Hz, 1H, ArH), 3.83 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 3.69 (s, 2H, CH_2), 3.18 (t, J=6.4 Hz, 2H, CH_2), 2.95 (t, J=6.4 Hz, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 158.7, 154.6, 151.6, 148.7, 147.9, 141.5, 126.4, 122.2, 121.7, 114.0, 111.1, 101.3, 55.5, 33.9, 25.0, 25.9. HRMS (ESI): m/z calcd for: $C_{17}H_{19}N_4O$, 295.1554, found: 295.1553.

4.2.30. 5-(3,4,5-Trimethoxyphenyl)-2,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridin-1-ol ***4ee***. Red solid, mp: 259–260 °C. IR (KBr, ν, cm^{-1}): 3067, 2935, 1649, 1579, 1509, 1459, 1415, 1243, 1128, 1004, 823, 681. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.96 (s, 1H, NH), 6.66 (s, 2H, ArH), 3.78 (s, 6H, OCH_3), 3.74 (s, 3H, OCH_3), 3.71 (s, 2H, CH_2), 3.19 (t, J=6.4 Hz, 2H, CH_2), 2.95 (t, J=6.8 Hz, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 158.6, 152.2, 141.5, 137.3, 129.5, 121.5, 107.4, 101.1, 60.0, 55.9, 34.0, 25.2, 25.0. HRMS (ESI): m/z calcd for: $C_{18}H_{20}N_3O_4S$, 374.1170, found: 374.1171.

4.2.31. 5-(4-Dimethylaminophenyl)-2,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridin-1-ol ***4ff***. Yellow solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3067, 2910, 1596, 1541, 1396, 1275, 1238, 1198, 1134, 948, 824, 630. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.88 (s, 1H, NH), 10.61 (s, 1H, OH), 7.21 (d, J=8.8 Hz, 2H, ArH), 6.81 (d, J=8.8 Hz, 2H, ArH), 3.69 (s, 2H, CH_2), 3.16 (t, J=6.4 Hz, 2H, CH_2), 2.98 (s, 6H, NCH_3), 2.94 (t, J=6.8 Hz, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 158.7, 157.1, 141.7, 137.3, 130.8, 130.0, 124.8, 115.6, 111.1, 101.1, 41.9, 34.0, 25.2, 24.9. HRMS (ESI): m/z calcd for: $C_{17}H_{19}N_4OS$, 327.1275, found: 327.1275.

4.2.32. 5-(Thiophen-2-yl)-2,6,8,9-tetrahydropyrazolo[3,4-b]thiopyrano[4,3-d]pyridin-1-ol ***4gg***. Yellow-green solid, mp: 298–299 °C. IR (KBr, ν, cm^{-1}): 3101, 2978, 1592, 1542, 1266, 1142, 852, 832. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 12.12 (s, 1H, NH), 7.76 (d, J=4.4 Hz, 1H, thienyl–H), 7.22–7.19 (m, 2H, thienyl–H), 3.73 (s, 2H, CH_2), 3.19 (t, J=6.4 Hz, 2H, CH_2), 2.95 (t, J=6.4 Hz, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 158.7, 154.2, 133.8, 129.5, 127.9, 127.1, 122.8, 112.7, 101.4, 33.9, 30.7, 25.1, 24.9. HRMS (ESI): m/z calcd for: $C_{13}H_{12}N_3OS_2$, 290.0417, found: 290.0411.

4.3. Typical procedure for the preparation of (*E*)-7-(4-chlorobenzylidene)-4-(4-chlorophenyl)-3-methyl-1-phenyl-1,5,6,7-tetrahydrocyclopenta[*b*]pyrazolo[4,3-*e*]pyridine 5a

In a 10-mL Emrys reaction vial, the 4-chlorobenzaldehyde (0.28 g, 2 mmol), cyclopentanone (0.08 g, 1 mmol), 3-methyl-1-phenyl-1*H*-pyrazol-5-amine (0.17 g, 1 mmol), NaOH (0.01 g, 0.2 mmol), and DMF (2.0 mL) were mixed and stirred at room temperature for 3 min. Then the mixture was heated for 15 min at 120 °C under microwave irradiation. The automatic mode stirring helped the mixing and uniform heating of the reactants. Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature. The solid product was collected by Büchner filtration and subsequently washed with ethanol to give the pale yellow solid.

Pale yellow solid, mp: 198–200 °C. IR (KBr, ν, cm^{-1}): 3048, 2918, 2842, 1595, 1572, 1501, 1491, 1340, 1288, 1195, 1090, 1016, 910, 826, 755, 691. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.41–8.33 (m, 2H, ArH), 7.91 (d, J=8.4 Hz, 1H, =CH), 7.68–7.59 (m, 8H, ArH), 7.53–7.49 (m, 2H, ArH), 7.33 (t, J=7.2 Hz, 1H, ArH), 3.14–3.13 (m, 2H, CH_2), 2.94–2.90 (m, 2H, CH_2), 2.04 (s, 3H, CH_3). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 152.1, 142.2, 141.8, 140.1, 139.8, 139.5, 135.9, 134.6, 134.4, 133.0, 131.7, 130.5, 130.1, 129.0, 128.8, 128.8, 125.4, 123.3, 120.9, 115.2, 29.4, 26.7, 15.0. HRMS (ESI): m/z calcd for: $C_{29}H_{22}Cl_2N_3$, 482.1186, found: 482.1183.

4.3.1. (E)-7-(3,4-Dichlorobenzylidene)-4-(3,4-dichlorophenyl)-3-methyl-1-phenyl-1,5,6,7-tetrahydrocyclopenta[b]pyrazolo[4,3-e]pyridine ***5b***. Brown solid, mp: 206–208 °C. IR (KBr, ν, cm^{-1}): 2924, 1593, 1568, 1504, 1381, 1194, 1136, 1092, 905, 817, 758, 691. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.38–8.36 (m, 2H, ArH), 7.68 (d, J=2.0 Hz, 1H, =CH), 7.66–7.63 (m, 2H, ArH), 7.61–7.58 (m, 2H, ArH), 7.56–7.54 (m, 2H, ArH), 7.52–7.49 (m, 1H, ArH), 7.44–7.42 (m, 1H, ArH), 7.36–7.32 (m, 1H, ArH), 3.23–3.18 (m, 2H, CH_2), 3.03–2.99 (m, 2H, CH_2), 2.19 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 143.2, 142.9, 141.9, 139.6, 135.8, 132.9, 130.7, 130.6, 130.5, 130.5, 129.1, 128.4, 128.0, 125.5, 123.1, 122.3, 121.0, 37.9, 29.4, 15.0. HRMS (ESI): m/z calcd for: $C_{29}H_{20}Cl_4N_3$, 550.0406, found: 550.0405.

4.3.2. (E)-3-Methyl-7-(4-methylbenzylidene)-1-phenyl-4-(p-tolyl)-1,5,6,7-tetrahydrocyclopenta[b]pyrazolo[4,3-e]pyridine ***5c***. Yellow solid, mp: 158–160 °C. IR (KBr, ν, cm^{-1}): 3011, 2921, 2854, 1596, 1570, 1555, 1507, 1410, 1341, 1287, 1181, 892, 816, 753, 687, 650, 517. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.40 (d, J=7.6 Hz, 2H, ArH), 7.71 (d, J=2.4 Hz, 1H, =CH), 7.54 (t, J=8.0 Hz, 2H, ArH), 7.50 (d, J=8.0 Hz, 2H, ArH), 7.34–7.28 (m, 5H, ArH), 7.23 (d, J=8.0 Hz, 2H, ArH), 3.22–3.18 (m, 2H, CH_2), 3.00–2.96 (m, 2H, CH_2), 2.47 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 2.14(s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 142.6, 140.5, 138.2, 137.2, 134.8, 133.1, 131.7, 129.3, 129.3, 129.1, 129.0, 128.7, 128.6, 125.1, 124.3, 120.8, 118.1, 115.3, 113.2, 29.5, 26.8, 21.4, 21.4, 15.0. HRMS (ESI): m/z calcd for: $C_{31}H_{28}N_3$, 442.2278, found: 442.2281.

4.3.3. 7-(4-Methoxybenzylidene)-4-(4-methoxyphenyl)-3-methyl-1-phenyl-1,5,6,7-tetrahydrocyclopenta[b]pyrazolo[4,3-e]pyridine ***5d***. Yellow solid, mp: 164–165 °C. IR (KBr, ν, cm^{-1}): 3000, 2933, 2837, 1602, 1508, 1296, 1251, 1172, 1033, 833, 759, 693, 646. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.44 (d, J=8.0 Hz, 4H, ArH), 7.91 (d, J=9.2 Hz, 2H, ArH), 7.70 (d, J=2.4 Hz, 1H, =CH), 7.51 (t, J=8.0 Hz, 2H, ArH), 7.35 (d, J=8.4 Hz, 1H, ArH), 7.25 (t, J=7.6 Hz, 1H, ArH), 7.06–7.05 (m, 2H, ArH), 6.98 (t, J=8.8 Hz, 1H, ArH), 3.93 (s, 3H,

OCH_3), 3.91 (s, 3H, OCH_3), 3.34 (t, J=7.2 Hz, 2H, CH_2), 3.22 (t, J=7.2 Hz, 2H, CH_2), 2.18 (s, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 160.0, 148.9, 141.9, 140.2, 135.6, 130.7, 130.6, 130.4, 130.1, 130.0, 129.0, 128.9, 128.9, 124.8, 121.2, 120.8, 120.4, 113.8, 113.7, 113.7, 55.4, 55.4, 31.6, 25.8, 14.1. HRMS (ESI): m/z calcd for: $C_{31}H_{28}N_3O_2$, 474.2178, found: 474.2180.

4.3.4. (E)-3-Methyl-1-phenyl-7-(3,4,5-trimethoxybenzylidene)-4-(3,4,5-trimethoxyphenyl)-1,5,6,7-tetrahydrocyclopenta[b]pyrazolo[4,3-e]pyridine ***5e***. Yellow solid, mp: 229–231 °C. IR (KBr, ν, cm^{-1}): 2936, 2835, 1578, 1508, 1413, 1303, 1239, 1127, 1006, 831, 765. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.40 (dd, J_1=1.2 Hz, J_2=8.6 Hz, 2H, ArH), 7.68 (t, J=2.8 Hz, 1H, =CH), 7.60–7.56 (m, 2H, ArH), 7.35–7.31 (m, 1H, ArH), 6.87 (s, 2H, ArH), 6.63 (s, 2H, ArH), 3.99 (s, 3H, OCH_3), 3.96 (s, 6H, OCH_3), 3.92 (s, 3H, OCH_3), 3.92 (s, 6H, OCH_3), 3.29–3.25 (m, 2H, CH_2), 3.08–3.05 (m, 2H, CH_2), 2.24 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 400 MHz) (δ, ppm): 153.3, 153.2, 153.0, 149.2, 141.9, 140.2, 138.8, 136.0, 130.6, 129.0, 128.9, 125.3, 124.9, 124.6, 121.0, 120.3, 113.7, 106.7, 106.5, 106.0, 61.0, 56.3, 56.3, 31.6, 25.8, 14.1. HRMS (ESI): m/z calcd for: $C_{35}H_{36}N_3O_6$, 594.2599, found: 594.2592.

4.3.5. 7-(4-Chlorobenzylidene)-4-(4-chlorophenyl)-2,5,6,7-tetrahydrocyclopenta[b]pyrazolo[4,3-e]pyridin-3-ol ***5f***. Yellow solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3136, 1586, 1491, 1267, 1212, 1092, 1014, 822, 515. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 12.01 (s, 1H, NH), 7.63 (d, J=8.8 Hz, 2H, ArH), 7.57 (dd, J_1=14.4 Hz, J_2=8.8 Hz, 4H, ArH), 7.50 (s, 1H, =CH), 7.49 (d, J=6.8 Hz, 2H, ArH), 3.17–3.11 (m, 2H, CH_2), 3.04–3.01 (m, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 167.6, 161.0, 154.4, 154.3, 142.6, 139.5, 135.8, 133.1, 131.7, 131.3, 130.6, 129.5, 128.6, 127.8, 121.5, 121.1, 28.9, 26.5. HRMS (ESI): m/z calcd for: $C_{22}H_{16}Cl_2N_3O$, 408.0665, found: 408.0684.

4.3.6. 7-(4-Bromobenzylidene)-4-(4-bromophenyl)-2,5,6,7-tetrahydrocyclopenta[b]pyrazolo[4,3-e]pyridin-3-ol ***5g***. Yellow solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3408, 2945, 1593, 1543, 1487, 1262, 1205, 1072, 1009, 900, 823. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.87 (s, 1H, NH), 7.69 (d, J=8.4 Hz, 1H, ArH), 7.66 (d, J=8.4 Hz, 2H, ArH), 7.62 (d, J=8.4 Hz, 1H, ArH), 7.54 (d, J=8.4 Hz, 1H, ArH), 7.51 (d, J=8.8 Hz, 1H, ArH), 7.46 (d, J=8.4 Hz, 3H, ArH, 2H, and =CH, 1H), 2.97 (t, J=7.6 Hz, 2H, CH_2), 2.83 (t, J=7.2 Hz, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 167.6, 161.1, 154.2, 154.0, 142.7, 139.6, 138.3, 136.1, 134.4, 131.7, 131.6, 131.5, 130.9, 130.7, 130.6, 126.9, 121.8, 121.6, 99.9, 34.1, 28.9, 23.6. HRMS (ESI): m/z calcd for: $C_{22}H_{16}Br_2N_3O$, 495.9655, found: 495.9650.

4.3.7. 7-(4-Methylbenzylidene)-4-(p-tolyl)-2,5,6,7-tetrahydrocyclopenta[b]pyrazolo[4,3-e]pyridin-3-ol ***5h***. Yellow solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3215, 2917, 1587, 1519, 1389, 1342, 1275, 1206, 1183, 811. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.90 (s, 1H, NH), 10.52 (s, 1H, OH), 7.49 (d, J=8.4 Hz, 2H, ArH), 7.47 (s, 1H, =CH), 7.44 (d, J=8.0 Hz, 2H, ArH), 7.29 (d, J=8.0 Hz, 2H, ArH), 7.25 (d, J=8.0 Hz, 2H, ArH), 3.15–3.09 (m, 2H, CH_2), 3.03–2.99 (m, 2H, CH_2), 2.39 (s, 3H, CH_3), 2.34 (s, 3H, CH_3). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 167.4, 154.4, 154.2, 139.8, 137.4, 132.3, 129.5, 128.2, 126.8, 120.5, 100.3, 34.2, 29.2, 23.6, 20.9. HRMS (ESI): m/z calcd for: $C_{24}H_{22}N_3O$, 368.1758, found: 368.1781.

4.3.8. 7-(4-Methoxybenzylidene)-4-(4-methoxyphenyl)-2,5,6,7-tetrahydrocyclopenta[b]pyrazolo[4,3-e]pyridin-3-ol ***5i***. Yellow solid, mp: 286–287 °C. IR (KBr, ν, cm^{-1}): 3211, 2931, 2836, 1591, 1510, 1390, 1287, 1250, 1207, 1177, 1030, 825, 585. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.80 (s, 1H, NH), 10.54 (s, 1H, OH), 7.54 (d, J=8.8 Hz, 2H, ArH), 7.51 (d, J=8.8 Hz, 2H, ArH), 7.45 (s, 1H, =CH), 7.04 (d, J=8.8 Hz, 2H, ArH), 7.01 (d, J=8.8 Hz, 2H, ArH), 3.83 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 3.12–3.09 (m, 2H, CH_2), 3.04–3.01 (m, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 161.6, 159.2, 158.5, 140.8, 139.2, 131.0, 130.5, 129.7, 129.1, 127.1, 122.4, 114.2, 113.1, 112.7, 101.9, 55.2, 55.1, 28.9, 26.8. HRMS (ESI): m/z calcd for: $C_{24}H_{22}N_3O_3$, 400.1656, found: 400.1654.

4.3.9. 8-(4-Chlorobenzylidene)-4-(4-chlorophenyl)-5,6,7,8-tetrahydro-2H-pyrazolo[3,4-b]quinolin-3-ol ***5j***. Brown solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3418, 3046, 2951, 2837, 1660, 1591, 1539, 1490, 1275, 1180, 1014, 830. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.86 (s, 1H, NH), 10.59 (s, 1H, OH), 7.98 (s, 1H, =CH), 7.54–7.47 (m, 6H, ArH), 7.40 (d, J=8.8 Hz, 2H, ArH), 2.84 (t, J=5.2 Hz, 2H, CH_2), 2.60 (t, J=5.6 Hz, 2H, CH_2), 1.70–1.65 (m, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 162.3, 140.7, 136.9, 136.0, 134.1, 131.6, 131.2, 128.4, 127.7, 126.5, 123.9, 122.9, 112.7, 106.9, 27.7, 26.8, 22.7. HRMS (ESI): m/z calcd for: $C_{23}H_{18}Cl_2N_3O$, 422.0822, found: 422.0826.

4.3.10. 4-(Thiophen-2-yl)-8-(thiophen-2-ylmethylene)-5,6,7,8-tetrahydro-2H-pyrazolo[3,4-b]quinolin-3-ol ***5k***. Brown solid, mp: >300 °C. IR (KBr, ν, cm^{-1}): 3418, 3225, 2943, 1584, 1225, 1085, 687. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.92 (s, 1H, NH), 10.59 (s, 1H, OH), 8.20 (s, 1H, =CH), 7.77–7.72 (m, 2H, thienyl–H), 7.40 (s, 1H, thienyl–H), 7.23–7.18 (m, 3H, thienyl–H), 2.91–2.70 (m, 4H, CH_2), 1.82–1.74 (m, 2H, CH_2). ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 162.3, 140.2, 136.2, 134.7, 133.1, 130.0, 129.3, 127.7, 127.5, 126.8, 124.3, 121.5, 112.7, 102.4, 30.7, 26.8, 22.2. HRMS (ESI): m/z calcd for: $C_{19}H_{16}N_3OS_2$, 366.0730, found: 366.0726.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.09.081.

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20. Crystal data for **4n**: $C_{22}H_{18}ClN_3S$, pale yellow, crystal dimension 0.48×0.19×0.18 mm, monoclinic, space group $P2(1)/c$, a=8.8731(9) Å, b=19.9044(18) Å, c=10.5292(11) Å, $\alpha=\gamma=90°$, β=96.6890(10)°, V=1846.9(3) Å^3, M_r=391.90, Z=4, D_c=1.409 Mg/m^3, λ=0.71073 Å, μ(Mo Kα)=0.332 mm^{-1}, F(000)=816, R=0.0459, wR_2=0.0972, S=1.023, largest diff. Peak and hole: 0.240 and −0.321 e/Å^3.
21. Crystal data for **5a**: $C_{29}H_{21}Cl_2N_3$, pale yellow, crystal dimension 0.21×0.12×0.07 mm, triclinic, space group $P-1$, a=9.3908(12) Å, b=10.9265(13) Å, c=13.3054(14) Å, α=79.800(2)°, β=74.9200(10)°, γ=64.5530(10)°, V=1187.0(2) Å^3, M_r=482.39, Z=2, D_c=1.350 Mg/m^3, λ=0.71073 Å, μ(Mo Kα)=0.297 mm^{-1}, F(000)=500, R=0.0641, wR_2=0.1347, S=1.028, largest diff. Peak and hole: 0.296 and −0.263 e/Å^3.