A Green Synthesis of Highly Functionalized 3-amino-2-phenylsulfonyl-1-alkyl/aryl-1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones and Their Reduction and Photophysical Studies

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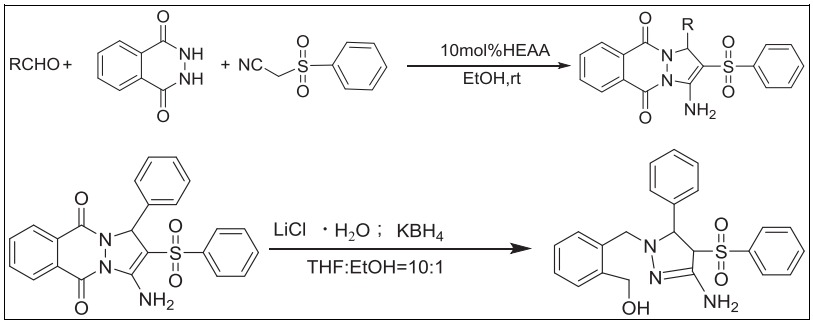

3-Amino-2-benzenesulfonyl-1-alkyl/aryl-1H-pyrazolo[1,2-b]phthalazine-5,10-dione derivatives were synthesized by the one-pot, three-component condensation of phthalhydrazide, aldehydes, and (phenylsulfonyl)acetonitrile in EtOH using 2-hydroxyethylammonium acetate as catalyst. The advantages of this method include environmental friendliness, easy work-up, and excellent yields. The reduction of some products and photophysical properties were also investigated.

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INTRODUCTION

Multicomponent reactions (MCRs) have attracted many attentions in organic, combinatorial, and medicinal chemistry and have been designed to produce elaborate biologically active compounds [1]. The MCR strategy offers significant advantages over conventional linear-type synthesis because of its convergence, atom efficient, operational simplicity, facile automation, easy work-up nature [2]. On the other hand, the synthesis of combinatorial small-molecule heterocyclic libraries has emerged as a valuable tool in the search for novel lead structures [3]. The success of combinatorial chemistry plays an important role in the discovery process of the new drug. Our studies show that the most promising and powerful method for generating combinatorial polyfunctionalized heterocyclic compounds is by sequential MCRs.

Heterocycles containing pyrazole ring have been found to be of broad pharmacological and biological interest such as cytotoxic [4], analgesic [5], antihyperglycemic [6], anti-inflammatory [7], antibacterial, [8] and antiviral activities [9]. Heterocycles fused with a phthalazine moiety are reported to possess anxiolytic [10], cytotoxic [11], anticonvulsant [12], antifungal [13], and anticancer [14].

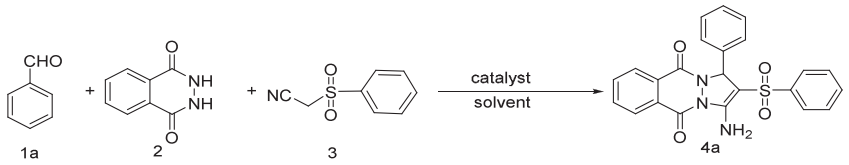
Sulfones are an important class of compounds present in many natural products due to their properties and reactivity [15], which possess wide spectrum of biological activities covering cytotoxic, anticancer, antimicrobic [16], anti-HIV [17], and trypanocidal [18]. Phenyl-substituted and heteroaryl-substituted sulfones are known as protecting group and important reactants in the Julia-type olefination reaction for the synthesis of variously useful intermediates and compounds [19]. In addition, some studies show that the sulfone functionalities can also be transformed into other useful functional groups [20]. Herein, considering the important biological properties of phthalazine derivatives and the powerful effect of MCRs, we wish to report a highly efficient, convenient, and facile method for synthesis of highly functionalized 3-amino-2-phenylsulfonyl-1-alkyl/aryl-1H-pyrazolo[1,2-b]phthalazine-5,10-diones derivatives via a three-component condensation reaction.

RESULTS AND DISCUSSION

At the onset of the research, we investigated the conversion of a mixture of benzaldehyde (**1a**) (1.0 mmol), phthalhydrazide (**2**) (1.0 mmol), and (phenylsulfonyl) acetonitrile [21] (**3**) (1.0 mmol) in different conditions. The reaction conditions were optimized, and the results were summarized in Table 1. Among all the catalysts tested in the solvent of EtOH at room temperature for 12 or 24 h (Table 1, entries 2–6), 2-hydroxyethylammonium acetate [$H_3N^+CH_2CH_2OH$]

Table 1

Optimization of the reaction condition for product **4a**[a].



1a 2 3 4a

Entry	Condition	Yield[b] (%)
1	No catalyst, C_2H_5OH, rt, 24 h	Trace
2	20 mol% L-Proline, C_2H_5OH,rt,12 h	56
3	20 mol% [bmim]OH,C_2H_5OH,rt, 12 h	83
4	20 mol% PTSA,C_2H_5OH,rt, 12 h	35
5	20 mol% Et_3N,C_2H_5OH, rt, 12 h	77
6	20 mol% HEAA,C_2H_5OH, rt, 12 h	86
7	20 mol% HEAA, DMF, rt, 12 h	63
8	20 mol% HEAA, CH_3CN, rt, 12 h	75
9	20 mol% HEAA, H_2O, rt, 24 h	Trace
10	10 mol% HEAA, C_2H_5OH, rt, 12 h	86
11	5 mol% HEAA, C_2H_5OH, rt, 12 h	74

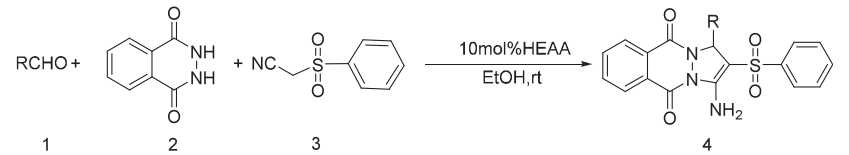
DMF, dimethylformamider; HEAA, hydroxyethylammonium acetate.
[a]The reaction was conducted with **1a** (1.0 mmol), **2** (1.0 mmol), **3** (1.0 mmol), and catalyst in 3.0 mL of solvent.
[b]Isolated yields.

[CH_3COO^-] (HEAA)[22] performed the best. EtOH turned out to be the optimal solvent as compared with dimethylformamide, MeCN, and H_2O (Table 1, entries 7–9). The catalyst HEAA loading of 5 mol% resulted in the formation of **4a** with 74% yield; however, when with 10 mol% catalyst, the yield significantly increased to 86%. No obvious improvement was observed by further increasing the catalyst loading to 20 mol%; 10 mol% catalyst was sufficient for this reaction. It is worthwhile to mention that when the reaction was stirred in water or without catalyst, only a trace amount of the product was formed even after prolonged heating.

The generality of this three-component reaction was studied under optimal conditions by various structures of aldehydes. The results were summarized in Table 2.

Table 2

Synthesis of 3-amino-2-phenylsulfonyl-1-alkyl/aryl-1H-pyrazolo[1,2-b]phthalazine-5,10-dione derivatives.



1 2 3 4

Entry	R	Products	Yield[b] (%)
1	C_6H_5	**4a**	86
2	4-Cl-C_6H_4	**4b**	94
3	4-F-C_6H_4	**4c**	90
4	3-Br-C_6H_4	**4d**	93
5	4-NO_2-C_6H_4	**4e**	96
6	4-CH_3-C_6H_4	**4f**	79
7	4-OH-C_6H_4	**4g**	80
8	4-isopropylC_6H_4	**4h**	84
9	4-MeO-C_6H_4	**4i**	76
10	CH_3	**4j**	65
11	*n*-C_3H_7	**4k**	70
12	*iso*-C_3H_7	**4l**	69
13	*iso*-C_4H_9	**4m**	61

[a]The reaction was conducted with **1** (1.0 mmol), **2** (1.0 mmol), **3** (1.0 mmol), and 10 mol% hydroxyethylammonium acetate in 3.0 mL of ethanol at room temperature for 12 h.
[b]Isolated yields.

Table 3

UV–visible and fluorescence data of the examined derivatives of **4**.

Compound	λ^{abs}(nm)	λ^{ext}(nm)	λ^{em}(nm)	ε (M^{-1} cm^{-1})	Δν (cm^{-1})	Φ_f^a
4a	351	351	489	31 400	8040.13	0.065
4c	349	349	488	47 200	8161.49	0.068
4e	345	345	486	30 200	8409.38	0.075
4f	352	352	490	22 900	8000.93	0.165
4i	353	353	492	47 400	8003.41	0.048

λ^{abs}(nm), absorbance maxima; λ^{ext}(nm), excitation wavelength; λ^{em}(nm), fluorescence maxima; ε, molar absorptivity; Δν, Stoke's lines.
[a]Reference: 9,10-diphenylanthracene with Φ = 1.00.

Generally, aromatic aldehydes were more active than aliphatic aldehydes in this reaction. Electronic effect of substituents on the phenyl ring of aromatic aldehydes was observed. The electron-withdrawing group substituted substrates gave relatively higher yields of the corresponding products than those with electron-donating groups. Moreover, no expected product was obtained when ketones were applied to this reaction.

We extended our study to find out the reduction of **4a**. There are numerous examples of desulfonylation via Julia-type elimination. Sodium and magnesium metals have been used for the various reductively desulfonylated reactions where they act as a source of reductant [23]. However, it was not envisioned that the reductive nature of sodium or magnesium metal could be used for the deprotection of the phenylsulfonyl group, and **4a** was cut into two parts that is **2** and **7**. Reductive reaction of **4a** using lithium chloride and potassium borohydride in EtOH/tetrahydrofuran (1:10) gave the corresponding hydride reductant **5** (Scheme 1). The proposed structure of compound **5** was further unequivocally confirmed by single crystal X-ray crystallography (Fig. 1) [24].

Electronic absorption and photoluminescent properties: UV–visible absorption and fluorescence emission spectra were measured at room temperature at 1×10^{-5} M. The solvents were all freshly distilled and deoxygenized before use.

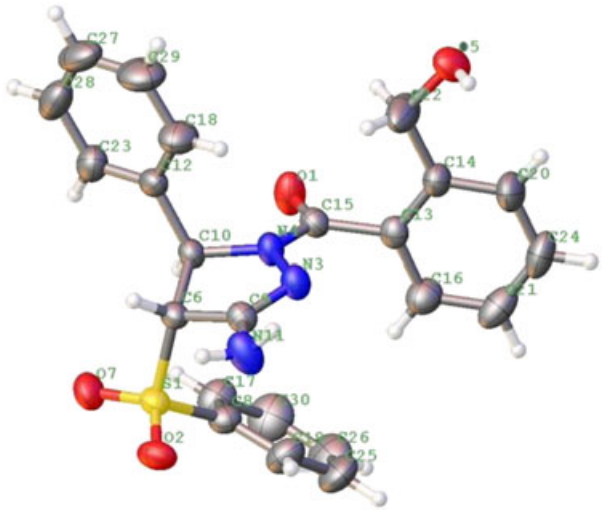
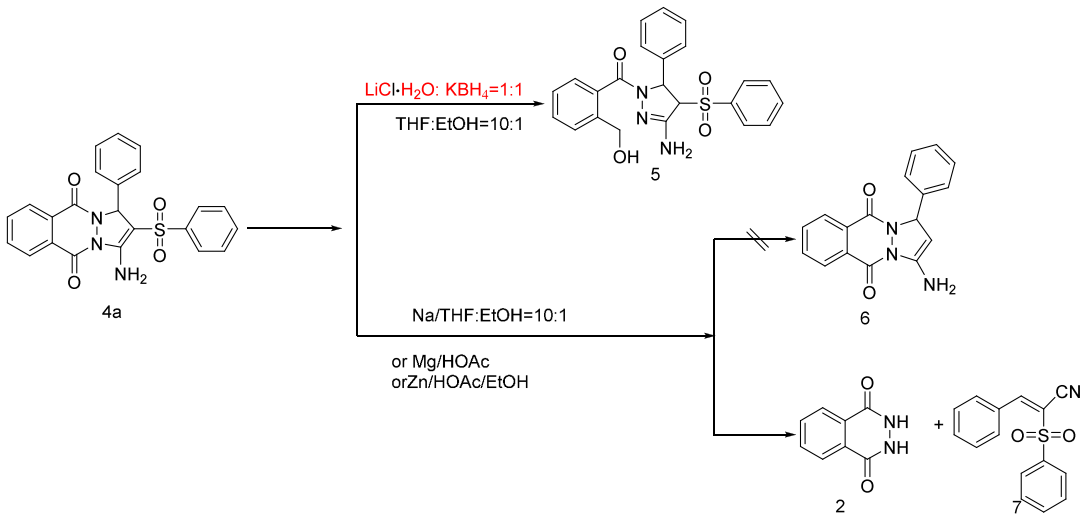


Figure 1. X-ray structure of compound **5**. [Color figure can be viewed at wileyonlinelibrary.com]

Scheme 1. The reduction of **4a**. [Color figure can be viewed at wileyonlinelibrary.com]



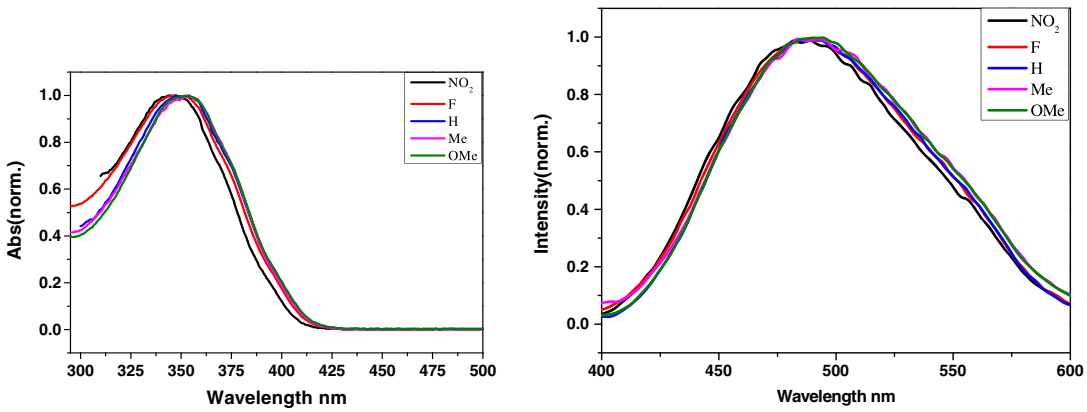


Figure 2. Absorption (left) and emission (right) spectra of **4e** (NO_2), **4c** (F), **4a** (H), **4f** (Me), and **4i** (OMe) and the dimethylsulfoxide as the solvent. [Color figure can be viewed at wileyonlinelibrary.com]

Five compounds were chosen which included the compound **4a** (H), **4f** (Me), **4i** (OMe), **4c** (F), and **4e** (NO_2). The absorption spectra (left) and emission spectra (right) in dimethylsulfoxide (DMSO) at 10^{-5} M concentrations was shown in Figure 2. Unexpectedly, no obvious electronic effects were seen both in absorption spectra and in emission spectra, just a main peak presented respectively. Both the main peak in absorption and emission spectra were attributed to the intrinsic value of the 1H-pyrazolo[1,2-b]phthalazine-5,10-dione nuclear. The contribution of strong electron-withdrawing group NO_2 in compound **4e** and F in compound **4c** was not apparently so did the strong electron-donating group Me in compound **4f** and OMe in compound **4i**, the probable reason was that the substituted phenyl ring in 1-position was not coplanar with its nucleus 1H-pyrazolo[1,2-b] phthalazine-5,10-dione, so the substituent located on the phenyl ring could not transfer electronic effect effectively to the nucleus.

Although the electronic effect was not apparent, but it existed to some extent. As seen in Figure 2, the maximum absorption peak of **4e** (NO_2), **4c** (F), **4a** (H), **4f** (Me), and **4i** (OMe) was 345, 349, 351, 352, and 353 nm, respectively, electron-withdrawing group NO_2 (**4e**) and F (**4c**) caused the blue shift, while the electron-donating group Me (**4f**) and OMe (**4i**) caused the red shift compared with H (**4a)**. Moreover, it was reasonable that NO_2 group caused a larger blue shift than that caused by F group, while the OMe group caused a larger red shift than that caused by Me group. Similarly, the regularity could be observed in emission spectra in Figure 2 (right). The maximum emission of **4e** (NO_2), **4c** (F), **4a** (H), **4f** (Me), and **4i** (OMe) was located at 486, 488, 489, 490, and 492 nm, respectively; the electron withdrawing groups NO_2 and F caused a blue shift, and the shift value caused by NO_2 was larger. The same phenomenon was seen when the groups changed to Me and OMe.

CONCLUSION

In summary, highly functionalized 1H-pyrazolo[1,2-b] phthalazine-5,10-dione derivatives are of great interest due to their potential biological and pharmacological activities. A series of well-defined 3-amino-1-phenyl-2-(phenylsulfonyl)-1H-pyrazolo-[1,2-b]phthalazine-5,10-dione was synthesized and fully characterized. Their reduction and photophysical properties were also studied, and the results obtained by the absorption and emissive spectra demonstrated a certain fluorescent structure–property relationship.

EXPERIMENTAL SECTION

General information. All chemicals and solvents (analytical grade) were received from commercial sources and used without further purification. Infrared (IR) spectra were recorded on a Nicolet 6700 spectrometer in KBr. ^{1}H nuclear magnetic resonance (NMR) (500 MHz) and ^{13}C NMR spectra (125 MHz) were recorded on an Avance III 500 NMR spectrometer (Bruker) using tetramethylsilane as internal standard and DMSO-d_6 as solvent. Low-resolution and high-resolution mass spectra were taken on an Agilent 6210 TOF LC/MS spectrometer using the electrospray ionization (ESI).

General procedures for the synthesis of compounds 4. The mixture of the aldehydes **1** (1.0 mmol), phthalhydrazide **2** (1.0 mmol), (phenylsulfonyl) acetonitrile **3** (1.0 mmol), and HEAA (0.1 mmol) in EtOH (3 ml) was stirred at room temperature for 12 h (monitored by thin-layer chromatography). After completion of the reaction, the solid product was collected by filtration and recrystallized from methanol to give the pure compound **4**. The ionic liquid HEAA was successively recovered extracting from the filtrate and reused.

3-Amino-2-(phenylsulfonyl)-1-phenyl-1H-pyrazolo2-[1,2-b] phthalazine-5,10-dione (4a). Yellow powder; IR (KBr) (vmax): 3463, 3336, 3065, 3303, 1645, 1396, 1290, 1130, 1097 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, δ): 8.29–8.21 (1H, m), 8.06–8.00 (1H, m), 7.98–7.78 (4H, m), 7.52–7.45 (1H, m), 7.42–7.40(2H, m), 7.35–7.28 (2H, m), 7.25–7.19 (2H, m), 7.19–7.08 (3H, m), 6.05 (1H, s); ^{13}C NMR (125 MHz,DMSO-d_6, δ): 157.44,153.21, 147.42, 142.94, 137.35, 134.70, 133.61, 132.29, 128.76, 128.73, 128.68, 127.90, 127.86, 127.59, 127.28, 126.55, 125.58, 84.89, 64.97; MS (ESI): ([M +H]$^+$) 432.1; HRMS (ESI) calcd for $C_{23}H_{17}N_3O_4S$ ([M + H]$^+$) 432.1018, found 432.1030.

3-Amino-2-phenylsulfonyl-1-(4-chloro-phenyl)-1H-pyrazolo-[1,2-b]phthalazine-5,10-dione (4b). Yellow powder; IR (KBr) (vmax): 3456, 3332, 3062,1635, 1395, 1300, 1135, 1094 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, δ): 8.28–8.22 (1H, m), 8.06–8.01 (1H, m), 7.97–7.93 (2H, m), 7.93–7.72 (2H, m), 7.54 (1H, t, J = 7.4 Hz), 7.49–7.43 (2H, m), 7.37 (2H, d, J = 7.5 Hz), 7.27 (2H, d, J = 8.4 Hz), 7.14 (2H, d, J = 8.4 Hz), 6.03 (1H, s); ^{13}C NMR (125 MHz, DMSO-d_6, δ): 157.44, 153.27, 147.55, 142.95, 136.47, 134.68, 133.65, 132.51, 132.32,129.47, 128.82, 128.73, 128.57, 127.79, 127.25, 126.52, 125.58, 84.51, 63.22; MS (ESI): ([M + H]$^+$) 466.1; HRMS (ESI) calcd for $C_{23}H_{16}ClN_3O_4S$ ([M + H]$^+$) 466.0628, found 466.0646.

3-Amino-2-phenylsulfonyl-1-(4-fluoro-phenyl)-1H-pyrazolo-[1,2-b]phthalazine-5,10-dione (4c). Yellow powder; IR (KBr) (vmax): 3435, 3320, 3020, 2895, 1640, 1395, 1300, 1140, 1095 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, δ): 8.25 (1H, m), 8.06–8.02 (1H, m), 7.95 (2H, m), 7.89 (2H, s), 7.53 (1H, t, J = 7.3 Hz), 7.46 (2H, d, J = 7.5 Hz), 7.36 (2H, t, J = 15.55 Hz), 7.27 (2H, m), 6.90 (2H, m), 6.05 (1H, s); ^{13}C NMR (125 MHz, DMSO-d_6, δ): 157.44, 153.25, 147.46, 143.00, 134.65, 133.61, 132.33, 129.73, 129.67, 128.80, 128.71, 128.63, 127.24, 126.51, 125.57, 114.64, 114.47, 84.57, 63.21; MS (ESI): ([M + H]$^+$) 450.1; HRMS (ESI) calcd for C23H16FN3O4S ([M + H]$^+$) 450.0924, found 450.0939.

3-Amino-2-phenylsulfonyl-1-(3-bromo-phenyl)-1H-pyrazolo-[1,2-b]phthalazine-5,10-dione (4d). Yellow powder; IR (KBr) (vmax): 3405, 3307, 3016, 2900, 1665, 1400, 1360, 1294, 1138, 1097 cm^{-1}; ^1H NMR (500 MHz, DMSO-d6, δ): 8.26–8.24 (1H, m), 8.07–8.03 (1H, m), 7.97–7.93 (2H, m), 7.91–7.87 (2H, m), 7.52 (1H, t, J = 7.3 Hz), 7.43 (2H, d, J = 7.3 Hz), 7.36–7.31 (5H, m), 7.11 (1H, t, J = 7.8 Hz), 6.03 (1H, s); ^{13}C NMR (125 MHz, DMSO-d6, δ): 157.50, 153.36, 147.62, 142.86, 139.77, 134.61, 133.63, 132.53, 132.48, 130.80, 130.14, 129.87, 128.97, 128.70, 128.55, 127.23, 127.17, 126.54, 125.45, 125.10, 121.53, 84.08, 63.39; MS (ESI): ([M + H]$^+$) 510.1; HRMS (ESI) calcd for $C_{23}H_{16}BrN_3O_4S$ ([M + H]$^+$) 510.0123, found 510.0141.

3-Amino-2-phenylsulfonyl-1-(4-nitro-phenyl)-1H-pyrazolo-[1,2-b]phthalazine-5,10-dione (4e). Yellow powder; IR (KBr) (vmax): 3460, 3336, 3025, 2894, 1642, 1396, 1352, 1294, 1134, 1097 cm^{-1}; ^1H NMR (500 MHz, DMSO-d6, δ): 8.28 (1H, dt, J = 5.8 Hz, 3.2), 8.03 (1H, dt, J = 7.3, 3.2 Hz), 7.99–7.87 (6H, m), 7.60–7.55 (2H, m), 7.52–7.46 (3H, m), 7.36–7.31 (2H, m), 6.15 (1H, s); ^{13}C NMR (125 MHz, DMSO-d6, δ): 157.47, 153.42, 147.86, 146.98, 144.87, 142.88, 134.72, 133.77, 132.42, 128.97, 128.89, 128.76, 128.39, 127.29, 126.57, 125.57, 123.00, 83.96, 63.06; MS (ESI): ([M + H]$^+$) 477.2; HRMS (ESI) calcd for $C_{23}H_{16}N_4O_6S$ ([M + H]$^+$) 477.0869, found 477.0882.

3-Amino-2-phenylsulfonyl-1-p-tolyl-1H-pyrazolo-[1,2-b] phthalazine-5,10-dione (4f). Yellow powder; IR (KBr) (vmax): 3457, 3339, 3057, 2919, 1653, 1399, 1372, 1293, 1132, 1100 cm^{-1}; ^1H NMR (500 MHz, DMSO-d6, δ): 8.25(1H, s), 8.03 (1H, d, J = 2.9 Hz), 7.95 (2H, d, J = 3.0 Hz), 7.82 (2H, s), 7.50 (1H, d, J = 6.9 Hz), 7.41 (2H, d, J = 7.3 Hz), 7.33 (2H, d, J = 7.4 Hz), 7.08 (2H, d, J = 7.6 Hz), 6.89 (2H, d, J = 7.4 Hz), 6.00 (1H, s), 2.23 (3H, s); ^{13}C NMR (125 MHz, DMSO-d6, δ): 157.38, 153.10, 147.28, 142.93, 137.18, 134.65, 134.41, 133.55, 132.14, 128.71, 128.62, 128.38, 127.47, 127.24, 126.49, 125.62, 85.15, 63.71, 20.60; MS (ESI): ([M + H]$^+$) 446.2; HRMS (ESI) calcd for $C_{24}H_{19}N_3O_4S$ ([M + H]$^+$) 446.1175, found 446.1171.

3-Amino-2-phenylsulfonyl-1-(4-hydroxy-phenyl)-1H-pyrazolo-[1,2-b]phthalazine-5,10-dione (4g). Yellow powder; IR (KBr) (vmax): 3447, 3356, 3324, 3062, 1674, 1396, 1350, 1295, 1137, 1097 cm^{-1}; ^1H NMR (500 MHz, DMSO-d6, δ): 9.35(1H, s), 8.24(1H, m), 8.04 (1H, m), 7.97–7.92 (2H, m), 7.79 (2H, s), 7.53–7.50 (1H, m), 7.45 (2H, dd, J = 8.3, 1.1 Hz), 7.35 (2H, dd, J = 8.1 Hz, 7.5), 6.98 (2H, m), 6.47 (2H, m), 5.96 (1H, s); ^{13}C NMR (125 MHz, DMSO-d6, δ): 157.37, 157.20, 153.04, 147.17, 142.99, 134.66, 133.51, 132.23, 128.84, 128.81, 128.66, 127.46, 127.22, 126.49, 125.69, 114.56, 85.19, 63.59.; MS (ESI): ([M + H]$^+$) 448.1; HRMS (ESI) calcd for $C_{23}H_{17}N_3O_5S$ ([M + H]$^+$) 448.0967, found 448.0986.

3-Amino-2-phenylsulfonyl-1-(4-isopropyl-phenyl)-1H-pyrazolo-[1,2-b]phthalazine-5,10-dione (4h). Yellow powder; IR (KBr) (vmax): 3444, 3317, 3059, 2953, 1665, 1411, 1373, 1298, 1131, 1079 cm^{-1}; ^1H NMR (500 MHz, DMSO-d6, δ): 8.27–88.23 (1H, m), 8.05–8.01 (1H, m), 7.97–7.93 (2H, m), 7.83 (2H, s), 7.47 (1H, t, J = 7.3 Hz), 7.36 (2H, m), 7.29 (2H, dd, J = 8.2, 7.5 Hz), 7.09 (2H, d, J = 8.1 Hz), 6.94 (2H, d, J = 8.1 Hz), 6.04 (1H, s), 2.79 (1H, dt, J = 13.8, 6.9 Hz), 1.16 (6H, dd, J = 6.9 Hz, 2.8);^{13}C NMR (125 MHz, DMSO-d6, δ):157.42, 153.16, 148.02, 147.28, 142.96, 134.67, 134.53, 133.59, 132.20, 128.72, 128.60, 127.48, 127.27, 126.54, 125.79, 125.61, 85.00, 63.74, 33.10, 23.90, 23.75.; MS (ESI): ([M + H]$^+$)

474.2; HRMS (ESI) calcd for $C_{26}H_{23}N_3O_4S$ ([M + H]$^+$) 474.1488, found 474.1504.

3-Amino-2-phenylsulfonyl-1-(4-methoxy-phenyl)-1H-pyrazolo-[1,2-b]phthalazine-5,10-dione (4i). Yellow powder; IR (KBr) (vmax): 3455, 3336, 3066, 3000, 2906, 1650, 1392, 1356, 1295, 1134, 1089 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d6, δ): 8.26–8.23 (1H, m), 8.05–8.01 (1H, m), 7.96–7.82 (2H, m), 7.82 (2H, s), 7.52–7.49 (1H, m), 7.43 (2H, m), 7.34 (2H, m), 7.10 (2H, m), 6.63 (2H, m), 6.00 (1H, s), 3.70 (3H, s); ^{13}C NMR (125 MHz, DMSO-d6, δ): 159.00, 157.40, 153.12, 147.23, 143.02, 134.66, 133.55, 132.26, 129.16, 128.88, 128.76, 128.71, 128.68, 127.24, 126.50, 125.67, 113.28, 85.00, 63.51, 55.09.; MS (ESI): ([M + H]$^+$) 462.2; HRMS (ESI) calcd for $C_{24}H_{19}N_3O_5S$ ([M + H]$^+$) 462.1124, found 462.1116.

3-Amino-2-phenylsulfonyl-1-methyl-1H-pyrazolo-[1,2-b] phthalazine-5,10-dione (4j). Yellow powder; IR (KBr) (vmax): 3446, 3322, 3166, 3018, 2898, 1659, 1397, 1368, 1299, 1140, 1079 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d6, δ): 8.18 (1H, m), 8.12 (1H, m), 7.97–7.87 (4H, m), 7.83–7.69 (2H, m), 7.68 (1H, m),7.63 (2H, m), 5.08 (1H, q, J = 5.9), 1.51(3H, d, J = 5.9 Hz); ^{13}C NMR (125 MHz, DMSO-d6, δ): 157.46, 153.55, 147.75, 143.22, 134.67, 133.48, 132.94, 132.52, 129.43, 128.80, 128.52, 127.12, 126.50, 125.83, 125.09, 83.99, 57.01, 19.45; MS (ESI): ([M + H]$^+$) 370.1; HRMS (ESI) calcd for $C_{18}H_{15}N_3O_4S$ ([M + H]$^+$) 370.0862, found 370.0875.

3-Amino-2-(phenylsulfonyl)-1-propyl-1H-pyrazolo[1,2-b] phthalazine-5,10-dione (4k). Yellow powder; IR (KBr) (vmax): 3410, 3298, 3075, 2963, 2931, 2871, 1657, 1401, 1362, 1299, 1134, 1086 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d6, δ): 8.21 (1H, m), 8.16 (1H, m), 8.01–7.93 (4H, m), 7.77 (2H, s), 7.70 (1H, m), 7.67–7.61 (2H, m), 5.22 (1H, t, J = 3.0), 2.29–2.15 (1H, m), 1.70–1.57 (1H, m), 1.01–0.88 (2H, m), 0.58 (3H, t, J = 7.3 Hz); ^{13}C NMR (125 MHz, DMSO-d6, δ): 157.48, 153.67, 148.09, 143.06, 134.82, 133.60, 133.03, 129.47, 128.62, 128.43, 127.25, 126.64, 125.98, 81.40, 60.83, 56.06, 32.27, 18.57, 14.88, 13.37; MS (ESI): ([M + H]$^+$) 398.2; HRMS (ESI) calcd for $C_{20}H_{19}N_3O_4S$ ([M + H]$^+$) 398.1175, found 398.1183.

3-Amino-2-phenylsulfonyl-1-isopropyl-1H-pyrazolo-[1,2-b] phthalazine-5,10-dione (4l). Yellow powder; IR (KBr) (vmax): 3430, 3283, 3061, 2959, 2873, 1632, 1401, 1357, 1287, 1130, 1083 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d6, δ): 8.23 (1H, m), 8.16 (1H, m), 8.04–7.93 (4H, m), 7.74–7.56 (5H, m), 5.09 (1H, d, J = 1.7 Hz), 2.32–2.25 (1H, m), 0.93 (3H, d, J = 7.0 Hz), 0.73 (3H, d, J = 7.0 Hz); ^{13}C NMR (125 MHz, DMSO-d6, δ): 157.86, 155.18, 149.15, 143.02, 134.85, 133.51, 132.90, 129.35, 128.74, 128.31, 127.26, 126.70, 125.88, 81.59, 64.87, 33.00, 19.50, 15.56; MS (ESI): ([M + H]$^+$) 398.1; HRMS (ESI) calcd for $C_{20}H_{19}N_3O_4S$ ([M + H]$^+$) 398.1175, found 398.1182.

3-Amino-2-phenylsulfonyl-1-isobutyl-1H-pyrazolo-[1,2-b] phthalazine-5,10-dione (4m). Yellow powder; IR (KBr) (vmax): 3455, 3316, 3076, 2960, 2870, 1658, 1401, 1370, 1285, 1134, 1099 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d6, δ): 8.23 (1H, dd, J = 1.5, 1.65 Hz), 8.17 (1H, dd, J = 1.6, 1.35 Hz), 8.00–7.94 (4H, m), 7.76 (2H, s), 7.71–7.68 (1H, m), 7.65–7.59 (2H, m), 5.18 (1H, t, J = 3.8 Hz), 2.03 (1H, ddd, J = 14.5, 8.7, 3.6), 1.71 (1H, dt, J = 14.5, 4.2 Hz), 1.62 (1H, dd, J = 13.0, 6.6 Hz), 0.70 (3H, d, J = 6.7 Hz), 0.64 (3H, d, J = 6.6 Hz); ^{13}C NMR (125 MHz, DMSO-d6, δ): 157.55, 153.94, 148.13, 142.92, 134.91, 133.62, 132.98, 129.45, 128.65, 128.24, 127.27, 126.62, 125.92, 82.22, 59.87, 23.66, 23.36, 22.39.; MS (ESI): ([M + H]$^+$) 412.1; HRMS (ESI) calcd for $C_{21}H_{21}N_3O_4S$ ([M + H]$^+$) 412.1331, found 412.1336.

Typical procedure for the synthesis of compound 5. ***(3-amino-5-phenyl-4-(phenylsulfonyl)-4,5-dihydro-1H-pyrazol-1-yl)(2-(hydroxymethyl)phenyl)methanone (5).*** A mixture of 3-amino-2-(phenylsulfonyl)-1-phenyl-1H-pyrazolo-[1,2-b] phthalazine-5,10-dione (**4a**) (1.0 mmol), lithium chloride (1.0 mmol), and potassium borohydride (2.0 mmol) in EtOH/tetrahydrofuran (1:10) (5.0 mL) was stirred at room temperature for 1 h. The reaction mixture was filtered, and the solvent evaporated in vacuo to give the crude product, which was purified by recrystallization from EtOH: H_2O = 1:1 to afford the compound **5** (93%) as a colorless transparent crystal; colorless transparent crystal IR(KBr) (vmax): 3440, 3325, 3274, 3181, 3063, 3033, 2949, 1650, 1614, 1597, 1399, 1309, 1134, 1082 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d6, δ): δ_H (500 MHz, DMSO): 8.06–8.02 (2H, m), 7.92 (1H, dd, J = 11.7, 4.3 Hz), 7.79 (2H, t, J = 7.8 Hz), 7.47 (1H, d, J = 7.7 Hz), 7.40 (2H, dd, J = 10.2, 4.5), 7.34 (2H, ddd, J = 12.9, 6.3, 2.5), 7.17 (1H, t, J = 7.3 Hz), 7.06 (2H, d, J = 7.3 Hz), 6.75–6.67 (1H, m), 6.42 (2H, s), 5.73 (1H, d, J = 2.5 Hz), 5.04 (1H, t, J = 5.7 Hz), 4.78 (1H, d, J = 2.6 Hz), 4.35 (1H, dd, J = 14.4, 5.6), 4.26 (1 H, dd, J = 14.4, 5.6); ^{13}C NMR (125 MHz, DMSO-d6, δ): 163.96, 150.20, 139.49, 138.25, 135.70, 135.27, 133.81, 129.90, 129.24, 129.14, 128.67, 128.24, 126.85, 126.05, 125.73, 125.05, 75.12, 61.78, 60.27; MS (ESI): ([M + H]$^+$) 436.1; HRMS (ESI) calcd for $C_{23}H_{22}N_3O_4S$ ([M + H]$^+$) 436.1331, found 436.1346.

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[24] CCDC 941272 contains the supplementary crystallographic data for compound 5.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.