# A Rapid and an Efficient Route to the One-pot, Multicomponent Synthesis of 1*H*-Pyrazolo[1,2-*b*]phthalazine-5,10-dione Ring Systems

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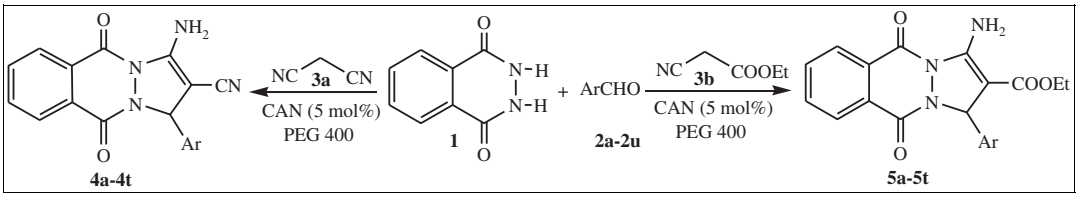


CAN is found to be an efficient catalyst for the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives via one-pot coupling reaction of phthalhydrazide, aromatic aldehydes, and malononitrile or ethyl cyanoacetate in PEG as solvent. The major attributes of this synthetic protocol are the use of nontoxic, inexpensive, and readily available catalyst, mild conditions, easy work up, improved yields, and the PEG 400 as solvent that is environmentally benign as well as recyclable.

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## INTRODUCTION

The rapid assembly of molecular diversity utilizing multicomponent reaction (MCRs) has received a great deal of attention, most notably for the construction of heterocyclic "drug-like" libraries [1–3]. These methodologies prove useful particularly when they lead to the formation of privileged medicinal heterocyclic scaffolds. Nitrogen-containing heterocyclic compounds are widespread in nature, and their applications to biologically active pharmaceuticals, agrochemicals, and functional materials are gaining prominence these days [4–6]. The development of new efficient methods to synthesize *N*-heterocycles with structural diversity is one of the major interests of modern synthetic chemists [7–9]. Among a large variety of nitrogen-containing heterocyclic compounds, heterocycles containing bridgehead hydrazine have attracted immense attention because of their pharmacological properties and clinical applications [10–15]. Similarly, pyrazole ring is a key fragment in numerous biologically active compounds [16–19]. Pyrazolo[1,2-*b*] phthalazine derivatives are known to possess a wide range of biological activities such as antihyperglycemic, antibacterial, antiviral, anti-inflammatory, analgesic, antihypoxic, and antipyretic activities [20,21]. So far, only a few methods have been reported for the synthesis of 1*H*-pyrazolo[1,2-*b*] phthalazine-diones [22]. Despite the available methods, there is still a need to develop a green as well as a convenient protocol for the efficient preparation of heterocycles containing a phthalazine ring fragment.

The use of CAN has recently received considerable attention as an inexpensive, nontoxic, commercially available catalyst for various organic transformations to afford the corresponding products in excellent yields. Because of the numerous advantages associated with this eco-friendly compound, CAN has been explored as a powerful catalyst for a variety of organic reactions [23].

The search for alternative reaction media to replace volatile and often toxic solvents commonly used in organic synthetic procedures is an important objective of significant environmental consequence. With the aim of improving the eco-sustainability of the fundamental organic transformations, recently, PEG has attracted great interest as a green and novel solvent for catalytic processes because it is relatively inexpensive, essentially nontoxic, readily available, and biodegradable material (PEG is approved for use in beverages) [24]. Various kinds of research have been reported involving PEG as a solvent or medium for organic synthesis [25].

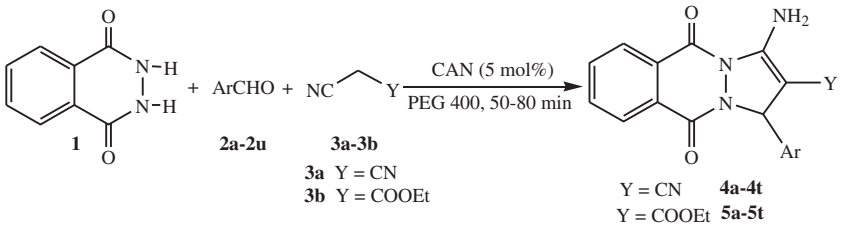
Because pyrazolo[1,2-*b*]phthalazine-dione derivatives are important biologically active compounds, which have potential medical applications, improvement and the development of a preparation of this type of compound by using CAN as a catalyst in reusable solvent PEG 400 were worthy of study.

## RESULTS AND DISCUSSION

In continuation of our interest towards the exploration of the catalytic potential of CAN in organic synthesis [26], and development of new greener synthetic methodologies [27], herein, we wish to report a one-pot, multicomponent synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives utilizing CAN as catalyst in PEG 400 as an eco-safe and recyclable solvent (Scheme 1).

We carried out an initial study in search for the optimal amount of CAN for the proposed transformation by using a model reaction involving phthalhydrazide **1**, benzaldehyde **2a**, and malononitrile **3a**, and the most significant data

**Scheme 1.** CAN-mediated synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones.




obtained is summarized in Fig. 1. It was observed that the yield of the final product increased with increasing amount of catalyst in the reaction mixture. The best result was obtained with 5 mol% of CAN, which gave the desired product in 92% yield after 50 min at 45°C. Further increase in the amount of CAN to 10 mol% decreased the product yield to 74%. A possible explanation for the low product yields is that the starting material or the product may have been destroyed during the reaction when excess amount (10 mol%) of CAN was used in the reaction [26].

We also investigated the role of solvents on the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives by using CAN as a catalyst. Among the various solvents, PEG 400 was found out to be the most appropriate solvent for this transformation and gave excellent yields (Table 1, entry 8).

To study the effect of temperature on this reaction, we also screened a range of temperatures for the model reaction, and the results are summarized in Table 2. Faster reactions occurred on increasing the reaction temperature, but the product yield decreased at high temperature because one of the reactants got oxidized at high temperature in the presence of CAN [26]. We found out that the reaction proceeded smoothly, and almost complete conversion of the product was observed at 45°C, affording **4a** in 92% yield within shorter time (Table 2, entry 2).

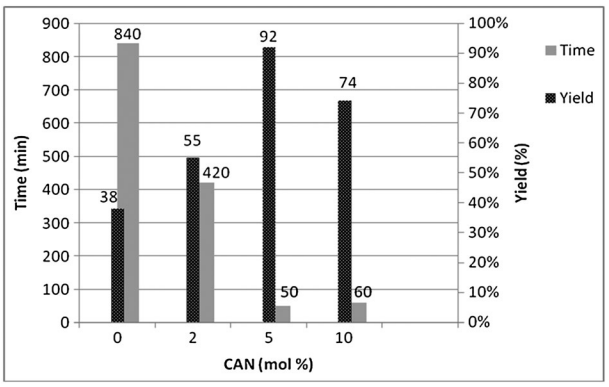



**Figure 1.** Catalytic activity evaluation of CAN for synthesis of 1*H*-pyrazolo [1,2-*b*]phthalazine-diones. Reaction conditions: phthalhydrazide **1** (1 mmol), benzaldehyde **2a** (1 mmol), malononitrile **3a** (1 mmol); catalyst: CAN (mol%); temperature: 45°C; solvent: PEG 400 (2mL). [a]Isolated yields.

To explore the scope and limitation of this reaction, we applied the optimized conditions and extended the reaction of phthalhydrazide **1** with a range of aromatic aldehydes **2a–2u** and malononitrile **3a** and ethyl cyanoacetate **3b** (Scheme 1) furnishing the respective 1*H*-pyrazolo[1,2-*b*] phthalazine-5,10-diones (**4a–4t**, **5a–5t**) in good to excellent yields (Table 3). The results were excellent in terms of yields and product purity by using aromatic aldehydes carrying electron-donating or electron-withdrawing substituents in the presence of CAN. Moreover, heterocyclic carbaldehydes were also well tolerated in the reaction and gave good results (Table 3, entries 18, 19, 20, 38, 39, and 40). Aliphatic

**Table 1**

Effect of various solvents on the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives.[a]

| Entry | Solvent (*x*) | Time (min) | Yield (%)[b] |
|---|---|---|---|
| 1 | MeOH | 100 | 82 |
| 2 | EtOH | 90 | 84 |
| 3 | THF | 450 | 62 |
| 4 | Toluene | 480 | 46 |
| 5 | MeCN | 150 | 78 |
| 6 | Ethylene glycol | 300 | 67 |
| 7 | PEG 200 | 60 | 90 |
| 8 | PEG 400 | 50 | 92 |
| 9 | PEG 600 | 50 | 92 |

[a]Reaction conditions: phthalhydrazide **1** (1 mmol), benzaldehyde **2a** (1 mmol), malononitrile **3a** (1 mmol); catalyst: CAN (5 mol%); temperature: 45°C; solvent: *x* (2 mL).
[b]Isolated yields.

**Table 2**

Effect of temperature.[a]

| Entry | Temp (°C) | Time (min) | Yield (%)[b] |
|---|---|---|---|
| 1 | 25 | 540 | 54 |
| 2 | 45 | 50 | 92 |
| 3 | 60 | 40 | 80 |
| 4 | 80 | 40 | 72 |

[a]Reaction conditions: phthalhydrazide **1** (1 mmol), benzaldehyde **2a** (1 mmol), malononitrile **3a** (1 mmol); catalyst: CAN (5 mol%); temperature: (°C); solvent: PEG 400 (2 mL).
[b]Isolated yields.

**Table 3**

CAN promoted synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones.[a]

| S. No. | Ar | *Y* | Product | Time (min) | mp (°C) | Yield (%)[b] |
|---|---|---|---|---|---|---|
| 1 | $C_6H_5$ (**2a**) | CN (**3a**) | **4a** | 50 | 274–276 [22b] | 92 |
| 2 | 4-Me-$C_6H_4$ (**2b**) | CN | **4b** | 50 | 190–194 [22b] | 92 |
| 3 | 4-MeO-$C_6H_4$ (**2c**) | CN | **4c** | 60 | 120–124 [22b] | 90 |
| 4 | 2-Cl-$C_6H_4$ (**2d**) | CN | **4d** | 60 | 258–262 [22b] | 87 |
| 5 | 3-Cl-$C_6H_4$ (**2e**) | CN | **4e** | 60 | 266–268 [22e] | 89 |
| 6 | 4-Cl-$C_6H_4$ (**2f**) | CN | **4f** | 50 | 266–270 [22b] | 90 |
| 7 | 4-Br-$C_6H_4$ (**2g**) | CN | **4g** | 70 | 256–260 [22e] | 86 |
| 8 | 2-$NO_2$-$C_6H_4$ (**2h**) | CN | **4h** | 75 | 264–266 [22e] | 85 |
| 9 | 3-$NO_2$-$C_6H_4$ (**2i**) | CN | **4i** | 70 | 160–164 [22b] | 86 |
| 10 | 4-$NO_2$-$C_6H_4$ (**2j**) | CN | **4j** | 65 | 130–134 [22b] | 88 |
| 11 | 2-HO-$C_6H_4$ (**2k**) | CN | **4k** | 65 | 172–174 | 87 |
| 12 | 3-HO-$C_6H_4$ (**2l**) | CN | **4l** | 60 | 232–236 | 90 |
| 13 | 4-HO-$C_6H_4$ (**2m**) | CN | **4m** | 50 | 292–296 | 91 |
| 14 | 4-$Me_2N$-$C_6H_4$ (**2n**) | CN | **4n** | 60 | 294–296 | 88 |
| 15 | $C_6H_5$-CH=CH (**2o**) | CN | **4o** | 55 | 120–124 | 86 |
| 16 | 2-HO-3-MeO-$C_6H_3$ (**2p**) | CN | **4p** | 50 | 152–154 | 84 |
| 17 | 1-Naphthyl (**2q**) | CN | **4q** | 65 | 182–184 | 85 |
| 18 | Piperonyl (**2r**) | CN | **4r** | 60 | 192–194 | 88 |
| 19 | 2-Furanyl (**2s**) | CN | **4s** | 70 | >300 | 86 |
| 20 | 2-Thienyl (**2t**) | CN | **4t** | 75 | 254–258 [22d] | 86 |
| 21 | $C_6H_5$ | COOEt (**3b**) | **5a** | 50 | 112–116 [22e] | 92 |
| 22 | 4-Me-$C_6H_4$ | COOEt | **5b** | 60 | 202–206 [22b] | 92 |
| 23 | 4-MeO-$C_6H_4$ | COOEt | **5c** | 60 | 146–150 | 87 |
| 24 | 2-Cl-$C_6H_4$ | COOEt | **5d** | 70 | 236–240 [22b] | 86 |
| 25 | 3-Cl-$C_6H_4$ | COOEt | **5e** | 60 | 210–214 [22e] | 89 |
| 26 | 4-Cl-$C_6H_4$ | COOEt | **5f** | 60 | 166–170 [22e] | 90 |
| 27 | 4-Br-$C_6H_4$ | COOEt | **5g** | 80 | 198–202 [22e] | 88 |
| 28 | 2-$NO_2$-$C_6H_4$ | COOEt | **5h** | 75 | 234–238 [22e] | 85 |
| 29 | 3-$NO_2$-$C_6H_4$ | COOEt | **5i** | 70 | 236–238 [22b] | 87 |
| 30 | 4-$NO_2$-$C_6H_4$ | COOEt | **5j** | 70 | 244–246 [22b] | 89 |
| 31 | 2-HO-$C_6H_4$ | COOEt | **5k** | 60 | 166–170 | 86 |
| 32 | 3-HO-$C_6H_4$ | COOEt | **5l** | 55 | 222–226 | 91 |
| 33 | 4-HO-$C_6H_4$ | COOEt | **5m** | 60 | >300 | 90 |
| 34 | 4-$Me_2N$-$C_6H_4$ | COOEt | **5n** | 65 | 5198–202 | 88 |
| 35 | $C_6H_5$-CH=CH | COOEt | **5o** | 60 | 182–186 | 85 |
| 36 | 4-HO-3-MeO-$C_6H_3$ (**2u**) | COOEt | **5p** | 60 | 286–290 | 85 |
| 37 | 1-Naphthyl | COOEt | **5q** | 60 | 134–138 | 87 |
| 38 | Piperonyl | COOEt | **5r** | 50 | 246–250 | 86 |
| 39 | 2-Furanyl | COOEt | **5s** | 65 | 272–274 | 88 |
| 40 | 2-Thienyl | COOEt | **5t** | 65 | >300 [22d] | 90 |

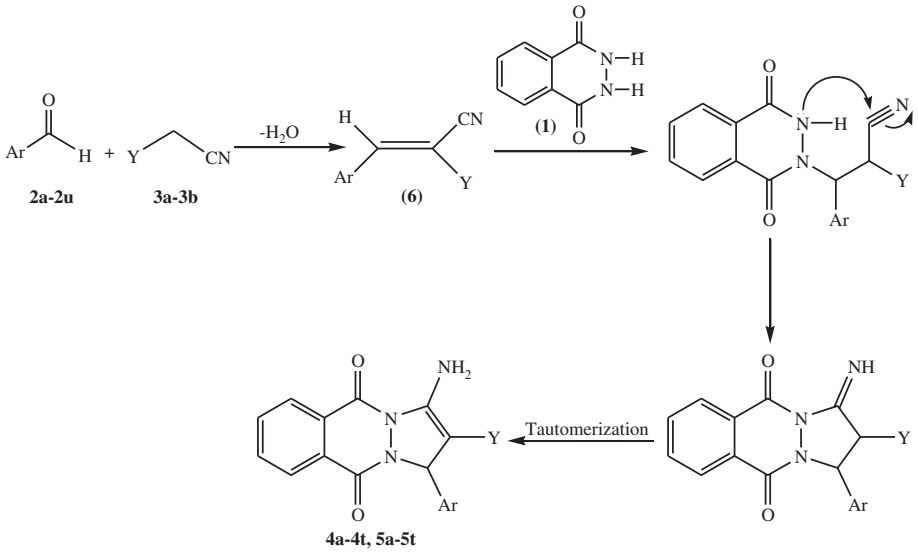
[a]Reaction conditions: phthalhydrazide **1** (1 mmol), aromatic aldehyde **2a–2u** (1 mmol), malononitrile **3a** or ethyl cyanoacetate **3b** (1 mmol); catalyst: CAN (5 mol%); temperature: 45°C; solvent: PEG 400 (2 mL).
[b]Isolated yields.

aldehydes were also utilized for the synthesis of 1*H*-pyrazolo [1,2-*b*]phthalazine-5,10-diones. Unfortunately, the catalyst was inactive for aliphatic substrates under the same reaction conditions, whereas without CAN, the reaction took longer time to complete (14 h) and gave only 38% of the desired product. (Fig. 1, Entry 1)

All the products (**4a–4t**, **5a–5t**) are stable solids and whose structures have been successfully deduced from their IR, $^1$H NMR, $^{13}$C NMR, and elemental analysis data. The mechanistic aspect of the reaction involves the initial formation of intermediate (**6**) by standard Knoevenagel condensation of the malononitrile **3a** or ethyl cyanoacetate **3b** and aldehyde **2a–2u**, which is followed by subsequent Michael-type addition of the phthalhydrazide (**1**) to the intermediate (**6**), which then undergoes cyclization and tautomerization to afford the corresponding products **4a–4t**, **5a–5t** (Scheme 2). To prove the reaction mechanism, a separate reaction of the Knoevenagel condensation product (**6**) and phthalhydrazide (**1**) was also run in parallel to the present model reaction. Both reactions gave the same product under the same reaction conditions, so both reaction pathways gave the same product.

Recycling experiments were also performed for the model reaction to establish the economic viability of solvent PEG 400, and the results are illustrated in Fig. 2. After completion of the reaction, the reaction mixture was kept in dry ice acetone bath to freeze the PEG and was extracted with ether (PEG being insoluble in ether). PEG 400 could be

**Scheme 2.** Suitable mechanism for the formation of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones.



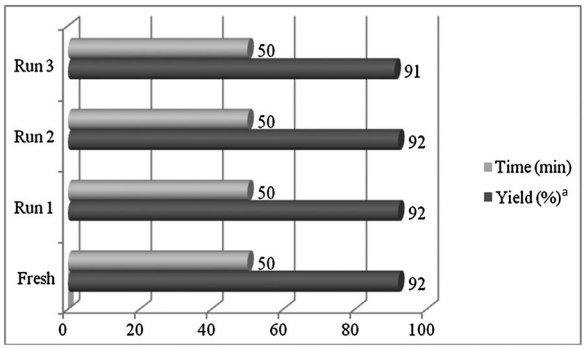




**Figure 2.** Recyclability of the solvent PEG 400. Reaction conditions: phthalhydrazide **1** (1 mmol), benzaldehyde **2a** (1 mmol), malononitrile **3a** (1 mmol); catalyst: CAN (5 mol%); temperature: 45°C; solvent: PEG 400 (2mL).[a]Isolated yields.

successfully recycled up to three runs, and the yields of the products were also comparable. Although a weight loss of ~4%–5% was observed from cycle to cycle because of mechanical loss, the percentages of PEG 400 recycled in each run were 100%, 97%, 92%, and 88% for fresh, Run 1, Run 2, and Run 3, respectively.

## CONCLUSION

In summary, we have developed an expedient and a clean protocol for the synthesis of 1*H*-pyrazolo[1,2-*b*] phthalazine-5,10-dione derivatives via cyclocondensation of aldehyde, malononitrile, or ethyl cyanoacetate and phthalhydrazide The one-pot nature and the use of CAN as an eco-friendly catalyst make it an interesting alternative to multistep approaches. Also, the solvent PEG 400 could be successfully recycled for at least three runs with consistent results. This method is quite simple, high yielding, time saving, and most importantly an eco-friendly process.

## EXPERIMENTAL

**Materials and methods.** All chemicals were purchased from Sigma-Aldrich (St. Louis, MO) and were used as such without further purification. All reactions and purity of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives were monitored by TLC using aluminium plates coated with silica gel $F_{254}$ plates (Merck) (Darmstadt, Germany) using 40% ethyl acetate and 60% hexane as an eluent. The spots were detected either under UV light or by placing in iodine chamber. Melting points were determined using a Thomas Hoover melting point apparatus (SECOR India Laboratory instruments, Delhi, India) and are uncorrected. IR spectra were recorded on a Perkin-Elmer FTIR-1710 spectrophotometer using KBr pellets/nujol film. $^1$H and $^{13}$C NMR spectra were recorded on a JEOL JNM-ECX 400P FT NMR spectrometer using TMS as an internal standard, and the value of chemical shifts are recorded on the δ scale, and coupling constants (*J*) values are in hertz (Hz). Elemental analysis was performed on a Hereaus CHN rapid analyzer. The temperature of the reaction mixture was measured through a noncontact infrared minigun thermometer (AZ minigun type, model 8868) (Shenzhen Laesent Technology Co. Ltd., Guangdong, China).

**General procedure for the synthesis of 1*H*-pyrazolo[1,2-*b*] phthalazine-5,10-dione derivatives.** In a 50 mL round-bottom flask, 1 equiv. each of phthalhydrazide **1**, aromatic aldehyde (ArCHO) **2a–2u**, and malononitrile **3a** or ethyl cyanoacetate **3b** in PEG 400 (2 mL) were mixed and stirred at 45°C. To this, CAN (5 mol%) was added and stirred for the appropriate time as indicated in Table 3. The progress of the reaction was monitored by TLC. To recycle PEG 400, after completion of the reaction, the reaction mixture was cooled with a dry ice–acetone bath to precipitate the PEG 400 and was extracted with ether (PEG being insoluble in ether). Thus, the PEG 400 remained as such and

which was then used for the subsequent reactions. The ether layer was decanted, dried, and concentrated under reduced pressure. The crude product thus obtained was subjected to purification by column chromatography on silica gel (100–200 mesh size) using hexane/ethyl acetate in varying proportions as eluent, which afforded the respective 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives, **4a–4t**, **5a–5t**. The recovered PEG 400 was reused for the consecutive runs. All the synthesized products were stable solids, and their structures were established on the basis of their spectral analysis (IR, $^1$H NMR, and $^{13}$C NMR) and elemental analysis data and melting point determination. The spectral data for synthesized compounds are listed in the following.

**Spectral data for the synthesized compounds.** ***3-Amino-5,10-dihydro-5,10-dioxo-1-phenyl-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4a).*** Light yellow solid, IR ($\nu_{max}$, KBr) 3361, 3165, 3014, 2198, 1661, 1492 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.22 (s, 1H, Ar–CH), 6.66 (br s, 2H, $NH_2$), 7.35–7.77 (m, 5H, Ar–H), 7.89–7.91 (m, 2H), 8.26–8.33 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 57.4, 82.9, 113.5, 126.6, 127.4, 129.6, 130.7, 130.9, 134.6, 142.6, 159.9, 162.3, 166.0; *Anal*. Calcd for $C_{18}H_{12}N_4O_2$: C, 68.35; H, 3.82; N, 17.71; found: C, 68.20; H, 3.60; N, 17.58.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(4-methylphenyl)-1H-pyrazolo [1,2-b]phthalazine-2-carbonitrile (4b).*** Light yellow solid, IR ($\nu_{max}$, KBr) 3368, 3035, 2919, 2225, 1674, 1652 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 2.43 (s, 3H, $CH_3$), 6.17 (s, 1H, Ar–CH), 6.67 (br s, 2H, $NH_2$), 7.30–7.70 (m, 4H, Ar–H), 7.77–7.80 (m, 2H), 8.23–8.32 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 22, 57.2, 81.2, 114, 127, 127.4, 128.4, 130.4, 130.9, 136.5, 146.4, 159.7, 162.7, 166.1; *Anal*. Calcd for $C_{19}H_{14}N_4O_2$: C, 69.08; H, 4.27; N, 16.96; found: C, 68.98; H, 4.14; N, 16.80.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(4-methoxyphenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4c).*** Yellow solid, IR ($\nu_{max}$, KBr) 3372, 3264, 2898, 2224, 1660, 1605 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 3.91 (s, 3H, $OCH_3$), 6.21 (s, 1H, Ar–CH), 6.91 (br s, 2H, $NH_2$), 7.00–7.65 (m, 4H, Ar–H), 7.90–7.92 (m, 2H), 8.25–8.34 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 54.3, 62.6, 86.4, 113.9, 114.4, 127.1, 128.0, 132.0, 132.9, 134.1, 158.9, 160.0, 161.9, 164.3; *Anal*. Calcd for $C_{19}H_{14}N_4O_3$: C, 65.89; H, 4.07; N, 16.18; found: C, 65.72; H, 3.95; N, 16.10.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(2-chlorophenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4d).*** Yellow solid, IR ($\nu_{max}$, KBr) 3372, 3160, 2224, 1678, 1634 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.41 (s, 1H, Ar–CH), 6.84 (br s, 2H, $NH_2$), 7.31–7.65 (m, 4H, Ar–H), 7.85–7.88 (m, 2H), 8.20–8.32 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 54.6, 79.6, 114.2, 126.8, 127.3, 127.8, 128.6, 129.2, 131.8, 132.4, 133.6, 143.6, 151.6, 162.7, 165.5; *Anal*. Calcd for $C_{18}H_{11}ClN_4O_2$: C, 61.64; H, 3.16; N, 15.97; found: C, 61.47; H, 3.00; N, 15.72.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(3-chlorophenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4e).*** Yellow solid, IR ($\nu_{max}$, KBr) 3366, 3190, 2217, 1674, 1646 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.24 (s, 1H, Ar–CH), 6.72 (br s, 2H, $NH_2$), 7.36–7.70 (m, 4H, Ar–H), 7.83–7.86 (m, 2H), 8.22–8.32 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 54.3, 81.4, 114.6, 124.8, 125.5, 126.9, 127.2, 128.8, 130.8, 131.6, 132.7, 141.6, 149.8, 159.3, 163.5; *Anal*. Calcd for $C_{18}H_{11}ClN_4O_2$: C, 61.64; H, 3.16; N, 15.97; found: C, 61.46; H, 2.95; N, 15.75.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(4-chlorophenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4f).*** Yellow solid, IR ($\nu_{max}$, KBr) 3376, 3094, 2229, 1652, 1586 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.18 (s, 1H, Ar–CH), 6.69 (br s, 2H, $NH_2$), 7.35–7.71 (m, 4H, Ar–H), 7.82–7.85 (m, 2H), 8.23–8.33 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 54.9, 81.8, 113.1, 126.9, 128.7, 128.9, 131.4, 131.7, 133.3, 140.0, 149.9, 158.5, 163.4, 165.5; *Anal*. Calcd for $C_{18}H_{11}ClN_4O_2$: C, 61.64; H, 3.16; N, 15.97; found: C, 61.50; H, 2.97; N, 15.68.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(4-bromophenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4g).*** Light brown solid, IR ($\nu_{max}$, nujol) 3367, 3312, 2921, 2190, 1694, 1581 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.19 (s, 1H, Ar–CH), 6.75 (br s, 2H, $NH_2$), 7.35–7.72 (m, 4H, Ar–H), 8.05–8.09 (m, 2H), 8.25–8.36 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 52.7, 69.7, 119.2, 121.2, 125.7, 129.3, 130.0, 131.4, 132.4, 142.4, 158.7, 162.7, 165.8; *Anal*. Calcd for $C_{18}H_{11}BrN_4O_2$: C, 54.70; H, 2.81; N, 14.18; found: C, 54.57; H, 2.74; N, 13.84.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(2-nitrophenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4h).*** Yellow solid, IR ($\nu_{max}$, KBr) 3385, 3188, 2915, 2213, 1698, 1658 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.52 (s, 1H, Ar–CH), 6.95 (br s, 2H, $NH_2$), 7.53–7.91 (m, 4H, Ar–H), 7.94–7.96 (m, 2H), 8.20–8.30 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 51.6, 78.8, 114.4, 122.8, 126.2, 126.7, 128.3, 129.4, 130.1, 132.4, 136.6, 142.8, 150.7, 158.8, 161.2; *Anal*. Calcd for $C_{18}H_{11}N_5O_4$: C, 59.84; H, 3.07; N, 19.38; found: C, 59.72; H, 2.92; N, 19.24.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(3-nitrophenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4i).*** Yellow solid, IR ($\nu_{max}$, nujol) 3348, 3221, 2920, 2232, 1702, 1617, 1533, 1351 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.74 (s, 1H, Ar–CH), 7.53–7.72 (m, 4H, Ar–H), 8.09 (br s, 2H, $NH_2$), 8.59–8.61 (m, 2H), 8.64–8.71 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 52.3, 62.5, 114.2, 121.6, 122.5, 127.7, 128.6, 131.6, 132.3, 133.5, 137.5, 148.5, 157.1, 162.0, 164.3; *Anal*. Calcd for $C_{18}H_{11}N_5O_4$: C, 59.84; H, 3.07; N, 19.38; found: C, 59.74; H, 2.95; N, 19.24.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(4-nitrophenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4j).*** Yellow solid, IR ($\nu_{max}$, nujol) 3403, 3238, 2915, 2193, 1718, 1658, 1522 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.39 (s, 1H, Ar–CH), 6.65 (br s, 2H, $NH_2$), 7.56–7.88 (m, 4H, Ar–H), 7.96–7.99 (m, 2H), 8.16–8.27 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 52.6, 60.1, 117.2, 122.7, 126.4, 128.3, 131.4, 132.9, 145.3, 147.5, 155.2, 162.3, 164.5; *Anal*. Calcd for $C_{18}H_{11}N_5O_4$: C, 59.84; H, 3.07; N, 19.38; found: C, 59.75; H, 3.10; N, 19.32.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(2-hydroxyphenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4k).*** Brown solid, IR ($\nu_{max}$, KBr) 3427, 3306, 2903, 2210, 1656, 1612 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.14 (s, 1H, Ar–CH), 6.62–6.97 (m, 4H, Ar–H), 7.75 (br s, 2H, $NH_2$), 7.86–7.90 (m, 2H), 8.22–8.30 (m, 2H), 10.86 (br s, 1H, OH); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 51.3, 82.6, 115.6, 118.7, 119.2, 126.5, 127.2, 127.8, 131.8, 132.3, 134.6, 148.4, 158.8, 160.7; *Anal*. Calcd for $C_{18}H_{12}N_4O_3$: C, 65.06; H, 3.64; N, 16.86; found: C, 64.93; H, 3.51; N, 16.74.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(3-hydroxyphenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4l).*** Light brown solid, IR ($\nu_{max}$, KBr) 3371, 3267, 2897, 2193, 1661, 1603 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 3.64 (br s, 1H, OH), 6.17 (s, 1H, Ar–CH), 6.68–7.02 (m, 4H, Ar–H), 7.72 (br s, 2H, $NH_2$), 7.87–7.91 (m, 2H), 8.27−8.36 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 61.6, 63.1, 113.5, 115.7, 117.3, 119.6, 125.2, 127.5, 129.5, 132.2, 133.6, 143, 156.5, 157.5, 160.1, 163.7; *Anal*. Calcd for $C_{18}H_{12}N_4O_3$: C, 65.06; H, 3.64; N, 16.86; found: C, 64.97; H, 3.43; N, 16.77.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(4-hydroxyphenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4m).*** Off white solid, IR ($\nu_{max}$, KBr) 3418, 3284, 2868, 2187, 1643, 1593 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$, 400 MHz, TMS) δ: 6.18 (s, 1H, Ar–CH), 6.70–7.08 (m, 4H, Ar–H), 7.67 (br s, 2H, $NH_2$), 7.84–7.86 (m, 2H), 8.23–8.32 (m, 2H), 10.60 (br s, 1H, OH); $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) δ: 54.2, 81.8, 116.7, 119.2, 126.7, 128.4, 129.6, 129.9, 132.4, 146.5, 157.3, 160.2, 164.8; *Anal*. Calcd for $C_{18}H_{12}N_4O_3$: C, 65.06; H, 3.64; N, 16.86; found: C, 64.91; H, 3.48; N, 16.75.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(4-dimethylaminophenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4n).*** Orange solid, IR ($\nu_{max}$, KBr) 3329, 3186, 2896, 2211, 1661, 1615 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 3.06 (s, 6H, 2 × $CH_3$), 6.24 (s, 1H, Ar–CH), 6.63–6.96 (m, 4H, Ar–H), 7.60 (br s, 2H, $NH_2$), 7.82–7.86 (m, 2H), 8.25–8.33 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 49.3, 54.8, 81.4, 114.2, 116.3, 127.8, 128.6, 129.4, 131.6, 133.7, 139.1, 147.6, 158.3, 162.7; *Anal*. Calcd for $C_{20}H_{17}N_5O_2$: C, 66.84; H, 4.77; N, 19.49; found: C, 66.75; H, 4.70; N, 19.37.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(styryl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4o).*** Brown solid, IR ($\nu_{max}$, nujol) 3327, 3170, 2918, 2226, 2197, 1684, 1606, 1577 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.22 (m, 1H, Ar–CH), 6.92 (m, 1H), 7.03 (d, 1 H, $J$ = 15.2 Hz), 7.36–7.62 (m, 5H, Ar–H), 7.76 (br s, 2H, $NH_2$), 7.86–7.91 (m, 2H), 8.26–8.37 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 60.3, 69.7, 113.1, 121.7, 126.6, 127.7, 128.4, 128.7, 131.5, 132.3, 133.4, 160.0, 162.6, 164.7; *Anal*. Calcd for $C_{20}H_{14}N_4O_2$: C, 70.17; H, 4.12; N, 16.37; found: C, 70.06; H, 4.02; N, 16.22.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(2-hydroxy-3-methoxyphenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4p).*** Dark green solid, IR ($\nu_{max}$, nujol) 3333, 3171, 2897, 2202, 1735, 1654, 1567 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.07 (s, 1H, Ar–CH), 3.65 (s, 3H, $OCH_3$), 7.04 (br s, 2H, $NH_2$), 7.15–7.35 (m, 3H, Ar–H), 7.76–7.83 (m, 2H), 8.24 (br s, 1H, OH), 8.40–8.44 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 47.5, 55.6, 60.5, 116.0, 119.7, 119.9, 120.2, 127.5, 131.0, 131.7, 132.2, 141.5, 147.3, 158.3, 160.2, 165.4; *Anal*. Calcd for $C_{19}H_{14}N_4O_4$: C, 62.98; H, 3.89; N, 15.46; found: C, 62.84; H, 3.76; N, 15.32.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(1-naphthyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4q).*** Yellow solid, IR ($\nu_{max}$, nujol) 3432, 3110, 2925, 2227, 1667, 1566 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.15 (s, 1H, Ar–CH), 7.65 (br s, 2H, $NH_2$), 7.32–7.94 (m, 7H, Ar–H), 7.98–8.02 (m, 2H), 8.18–8.26 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 54.6, 85.3, 115.2, 122.4, 124.6, 124.9, 125.3, 125.8, 126.2, 127.4, 128.5, 130.8, 131.3, 132.6, 135.8, 137.6, 154.7, 158.4, 163.4; *Anal*. Calcd for $C_{22}H_{14}N_4O_2$: C, 72.12; H, 3.85; N, 15.29; found: C, 72.04; H, 3.72; N, 15.20.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(1-benzo[1,3]-dioxol-5-yl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4r).*** Yellow solid, IR ($\nu_{max}$, KBr) 3448, 2923, 2227, 1654, 1571 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 5.98 (s, 2H), 6.24 (s, 1H, Ar–CH), 6.76–6.92 (m, 3H, Ar–H), 7.82–7.85 (m, 2H), 8.14 (br s, 2H, $NH_2$), 8.22–8.32 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 59.9, 81.8, 100.2, 109.3, 112.8, 115.6, 119.8, 125.4, 128.7, 129.6, 133.2, 137.8, 140.2, 147.6, 156.1, 160.2; *Anal*. Calcd for $C_{19}H_{12}N_4O_4$: C, 63.33; H, 3.36; N, 15.55; found: C, 63.24; H, 3.26; N, 15.42.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(2-furanyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4s).*** Gray solid, IR ($\nu_{max}$, KBr) 3352, 3165, 2896, 2224, 1661, 1560 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.17 (s, 1H, Ar–CH), 6.64–6.92 (m, 3H, Ar–H), 7.46 (br s, 2H, $NH_2$), 7.80–7.84 (m, 2H), 8.14–8.23 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 58.1, 82.3, 107.6, 113.7, 118.2, 127.2, 128.6, 129.7, 137.6, 143.5, 151.4, 158.2, 162.3; *Anal*. Calcd for $C_{16}H_{10}N_4O_3$: C, 62.74; H, 3.29; N, 18.29; found: C, 62.62; H, 3.16; N, 18.18.

***3-Amino-5,10-dihydro-5,10-dioxo-1-(2-thienyl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4t).*** Green solid, IR ($\nu_{max}$, KBr) 3423, 3164, 2890, 2210, 1654, 1587 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 6.10 (s, 1H, Ar–CH), 6.77–6.95 (m, 3H, Ar–H), 7.54 (br s, 2H, $NH_2$), 7.78–7.84 (m, 2H), 8.20–8.32 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 56.7, 83.2, 113.8, 122.8, 124.1, 125.7, 127.7, 129.6, 131.3, 136.5, 144.8, 153.9, 158.0; *Anal*. Calcd for $C_{16}H_{10}N_4O_2S$: C, 59.62; H, 3.13; N, 17.38; found: C, 59.50; H, 3.06; N, 17.31.

***Ethyl-3-amino-5,10-dihydro-1-phenyl-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5a).*** Yellow solid, IR ($\nu_{max}$, nujol) 3449, 3020, 2917, 2227, 1727, 1673, 1655, 1598 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.38 (t, 3H, $^3J_{HH}$ = 7.30 Hz, $CH_3$), 4.37 (q, 2H, $^3J_{HH}$ = 7.30 Hz, $OCH_2$), 6.24 (s, 1H, Ar–CH), 6.84 (br s, 2H, $NH_2$), 7.33–7.56 (m, 5H, Ar–H), 7.96–7.98 (m, 2H), 8.23–8.28 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 12.9, 59.2, 61.3, 69.0, 124.1, 127.1, 128.0, 129.6, 131.0, 132.1, 142.4, 149.5, 160.8, 165.0, 165.4; *Anal*. Calcd for $C_{20}H_{17}N_3O_4$: C, 66.11; H, 4.72; N, 11.56; found: C, 66.03; H, 4.63; N, 11.40.

***Ethyl-3-amino-5,10-dihydro-1-(4-methylphenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5b).*** Yellow solid, IR ($\nu_{max}$, nujol) 3442, 3310, 3284, 2919, 2219, 1722, 1667, 1632 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.39 (t, 3H, $^3J_{HH}$ = 7.30 Hz, $CH_3$), 2.43 (s, 3H, $CH_3$), 4.38 (q, 2H, $^3J_{HH}$ = 7.30 Hz, $OCH_2$), 6.25 (s, 1H, Ar–CH), 7.30–7.54 (m, 4H, Ar–H), 7.89–7.91 (m, 2H), 8.04 (br s, 2H, $NH_2$), 8.22–8.30 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 13.8, 21.5, 62.2, 70.0, 101.1, 127.2, 128.4, 128.6, 129.7, 130.8, 135.7, 144.3, 154.6, 162.3, 164.7, 165.8; *Anal*. Calcd for $C_{21}H_{19}N_3O_4$: C, 66.83; H, 5.07; N, 11.13; found: C, 66.59; H, 4.90; N, 10.91.

***Ethyl-3-amino-5,10-dihydro-1-(4-methoxyphenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5c).*** Yellow solid, IR ($\nu_{max}$, nujol) 3387, 3156, 2916, 2254, 1774, 1723, 1594 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.36 (t, 3H, $^3J_{HH}$ = 7.30 Hz, $CH_3$), 3.86 (s, 3H, $OCH_3$), 4.34 (q, 2H, $^3J_{HH}$ = 7.30 Hz, $OCH_2$), 6.26 (s, 1H, Ar–CH), 6.89–7.74 (m, 4H, Ar–H), 7.80–7.84 (m, 2H), 8.14 (br s, 2H, $NH_2$), 8.24–8.34 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 13.4, 54.8, 60.3, 98.3, 114.0, 122.2, 123.4, 131.1, 133.1, 153.5, 162.1, 163.0, 163.7, 168.6; *Anal*. Calcd for $C_{21}H_{19}N_3O_5$: C, 64.12; H, 4.87; N, 10.68; found: C, 64.17; H, 4.79; N, 10.62.

***Ethyl-3-amino-5,10-dihydro-1-(2-chlorophenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5d).*** Yellow solid, IR ($\nu_{max}$, KBr) 3430, 3310, 3126, 2930, 2253, 1778, 1732, 1695, 1654, 1633 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.36 (t, 3H, $^3J_{HH}$ = 7.30 Hz, $CH_3$), 4.35 (q, 2H, $^3J_{HH}$ = 7.32 Hz, $OCH_2$), 6.18 (s, 1H, Ar–CH), 6.84–7.42 (m, 4H, Ar–H), 7.81 (br s, 2H, $NH_2$), 7.88–7.92 (m, 2H), 8.18–8.26 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 13.5, 46.2, 61.3, 72.5, 125.8, 126.2, 126.9, 128.2, 128.8, 129.1, 130.3, 132.6, 140.4, 147.4, 155.3, 159.7, 162.8; *Anal*. Calcd for $C_{20}H_{16}ClN_3O_4$: C, 60.38; H, 4.05; N, 10.56; found: C, 60.22; H, 3.91; N, 10.41.

***Ethyl-3-amino-5,10-dihydro-1-(3-chlorophenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5e).*** Yellow solid, IR ($\nu_{max}$, nujol) 3453, 3342, 3066, 2926, 2244, 1704, 1669, 1648 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.32 (t, 3H, $^3J_{HH}$ = 7.32 Hz, $CH_3$), 4.34 (q, 2H, $^3J_{HH}$ = 7.32 Hz, $OCH_2$), 6.10 (s, 1H, Ar–CH),

7.12–7.56 (m, 4H, Ar–H), 7.74 (br s, 2H, $NH_2$), 7.86–7.88 (m, 2H), 8.18–8.26 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 13.8, 54.1, 60.8, 72.3, 123.8, 125.3, 126.4, 127.1, 129.3, 131.2, 132.0, 134.2, 141.3, 149.0, 156.5, 158.7, 161.7; *Anal*. Calcd for $C_{20}H_{16}ClN_3O_4$: C, 60.38; H, 4.05; N, 10.56; found: C, 60.18; H, 3.89; N, 10.43.

***Ethyl-3-amino-5,10-dihydro-1-(4-chlorophenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5f).*** Light brown solid, IR ($\nu_{max}$, nujol) 3448, 3334, 3066, 2925, 2249, 1793, 1727, 1704, 1669, 1648 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.34 (t, 3H, $^3J_{HH}$ = 7.32 Hz, $CH_3$), 4.33 (q, 2H, $^3J_{HH}$ = 7.30 Hz, $OCH_2$), 6.16 (s, 1H, Ar–CH), 7.07–7.69 (m, 4H, Ar–H), 7.77 (br s, 2H, $NH_2$), 7.86–7.88 (m, 2H), 8.14–8.27 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 13.9, 53.7, 62.7, 70.5, 127.4, 128.1, 129.3, 129.5, 132.0, 134.3, 148.6, 162.5, 163.0, 165.1, 168.0; *Anal*. Calcd for $C_{20}H_{16}ClN_3O_4$: C, 60.38; H, 4.05; N, 10.56; found: C, 60.20; H, 3.93; N, 10.44.

***Ethyl-3-amino-5,10-dihydro-1-(4-bromophenyl)-5,10-dioxo-1H-pyrazolo[1,2-b] phthalazine-2-carboxylate (5g).*** Yellow solid, IR ($\nu_{max}$, nujol) 3448, 3322, 3165, 2876, 2225, 1722, 1667, 1631 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.40 (t, 3H, $^3J_{HH}$ = 7.30 Hz, $CH_3$), 4.38 (q, 2H, $^3J_{HH}$ = 7.30 Hz, $OCH_2$), 6.22 (s, 1H, Ar–CH), 7.31–7.65 (m, 4H, Ar–H), 7.84–7.86 (m, 2H), 8.18 (br s, 2H, $NH_2$), 8.24–8.35 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 13.2, 61.8, 69.3, 71.8, 124.6, 127.1, 129.4, 130.3, 131.4, 131.6, 141.7, 152.6, 160.9. 163.2, 165.8; *Anal*. Calcd for $C_{20}H_{16}BrN_3O_4$: C, 54.31; H, 3.65; N, 9.50; found: C, 54.18; H, 3.55; N, 9.37.

***Ethyl-3-amino-5,10-dihydro-1-(2-nitrophenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5h).*** Yellow solid, IR ($\nu_{max}$, KBr) 3452, 3328, 2895, 1710, 1663, 1644 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.43 (t, 3H, $^3J_{HH}$ = 7.32 Hz, $CH_3$), 4.45 (q, 2H, $^3J_{HH}$ = 7.32 Hz, $OCH_2$), 6.56 (s, 1H, Ar–CH), 7.53–7.82 (m, 4H, Ar–H), 7.88–7.92 (m, 2H), 8.30 (br s, 2H, $NH_2$), 8.35–8.42 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 13.7, 46.0, 57.8, 74.2, 121.8, 125.4, 126.7, 128.0, 130.1, 131.6, 134.2, 138.6, 145.8, 151.3, 159.6, 161.2, 164.3; *Anal*. Calcd for $C_{20}H_{16}N_4O_6$: C, 58.82; H, 3.95; N, 13.72; found: C, 58.72; H, 3.77; N, 13.58.

***Ethyl-3-amino-5,10-dihydro-1-(3-nitrophenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5i).*** Yellow solid, IR ($\nu_{max}$, KBr) 3422, 3307, 2898, 1719, 1680, 1664, 1607 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.42 (t, 3H, $^3J_{HH}$ = 7.32 Hz, $CH_3$), 4.43 (q, 2H, $^3J_{HH}$ = 7.30 Hz, $OCH_2$), 6.35 (s, 1H, Ar–CH), 7.50–7.82 (m, 4H, Ar–H), 7.87–7.89 (m, 2H), 8.31 (br s, 2H, $NH_2$), 8.37–8.43 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 13.2, 62.0, 63.7, 99.2, 124.3, 124.5, 126.0, 129.7, 131.3, 131.9, 147.4, 151.2, 154.6, 160.4, 165.0, 166.7; *Anal*. Calcd for $C_{20}H_{16}N_4O_6$: C, 58.82; H, 3.95; N, 13.72; found: C, 58.71; H, 3.81; N, 13.61.

***Ethyl-3-amino-5,10-dihydro-1-(4-nitrophenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5j).*** Yellow solid, IR ($\nu_{max}$, KBr) 3446, 3331, 2905, 1719, 1702, 1659, 1626, 1518 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.42 (t, 3H, $^3J_{HH}$ = 7.36 Hz, $CH_3$), 4.43 (q, 2H, $^3J_{HH}$ = 7.32 Hz, $OCH_2$), 6.33 (s, 1H, Ar–CH), 7.53–7.82 (m, 4H, Ar–H), 7.87–7.89 (m, 2H), 8.24 (br s, 2H, $NH_2$), 8.32–8.41 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 14.2, 59.8, 63.2, 70.4, 123.6, 124.3, 127.8, 131.5, 133.8, 145.7, 147.7, 151.7, 154.0, 157.1, 161.4; *Anal*. Calcd for $C_{20}H_{16}N_4O_6$: C, 58.82; H, 3.95; N, 13.72; found: C, 58.70; H, 3.84; N, 13.59.

***Ethyl-3-amino-5,10-dihydro-5,10-dioxo-1-(2-hydroxyphenyl)-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5k).*** Yellow solid, IR ($\nu_{max}$, KBr) 3422, 3312, 2876, 1742, 1663, 1487, 1298, 1081, 856, 791 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.34 (t, 3H, $^3J_{HH}$ = 7.32 Hz, $CH_3$), 4.26 (q, 2H, $^3J_{HH}$ = 7.30 Hz, $OCH_2$), 6.16 (s, 1H, Ar–CH), 6.88–7.62 (m, 4H, Ar–H), 7.86–7.89 (m, 2H), 8.33–8.41 (m, 2H), 8.53 (br s, 2H, $NH_2$), 11.01 (br s, 1H, OH); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 13.7, 38.9, 69.6, 72.2, 114.8, 122.2, 127.2, 127.9, 128.6, 128.7, 129.1, 131.7, 152.9, 153.3, 156.6, 161.6, 168.5; *Anal*. Calcd for $C_{20}H_{17}N_3O_5$: C, 63.32; H, 4.52; N, 11.08; found: C, 63.17; H, 4.39; N, 10.97.

***Ethyl-3-amino-5,10-dihydro-1-(3-hydroxyphenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5l).*** Yellow solid, IR ($\nu_{max}$, nujol) 3467, 3286, 2872, 2226, 1725, 1655, 1624 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.33 (t, 3H, $^3J_{HH}$ = 6.6 Hz, $CH_3$), 4.31 (q, 2H, $^3J_{HH}$ = 6.6 Hz, $OCH_2$), 6.16 (s, 1H, Ar–CH), 6.85–7.04 (m, 4H, Ar–H), 7.78 (br s, 2H, $NH_2$), 7.85–7.88 (m, 2H), 8.22–8.32 (m, 2H), 9.88 (br s, 1H, OH); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 14.1, 62.8, 63.9, 87.2, 115.6, 116.1, 119.6, 124.5, 129.0, 130.5, 132.5, 145.2, 155.8, 156.6, 162.5, 165.0, 165.3; *Anal*. Calcd for $C_{20}H_{17}N_3O_5$: C, 63.32; H, 4.52; N, 11.08; found: C, 63.20; H, 4.42; N, 10.92.

***Ethyl-3-amino-5,10-dihydro-1-(4-hydroxyphenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5m).*** Pale yellow solid, IR ($\nu_{max}$, nujol) 3450, 3265, 2896, 2233, 1733, 1662, 1589 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$, 400 MHz, TMS) δ: 1.37 (t, 3H, $^3J_{HH}$ = 6.8 Hz, $CH_3$), 4.34 (q, 2H, $^3J_{HH}$ = 6.6 Hz, $OCH_2$), 6.19 (s, 1H, Ar–CH), 6.90–7.20 (m, 4H, Ar–H), 7.65 (br s, 2H, $NH_2$), 7.83–7.86 (m, 2H), 8.20–8.30 (m, 2H), 9.68 (br s, 1H, OH); $^{13}$C NMR (DMSO-$d_6$, 100 MHz) δ: 13.5, 55.2, 61.1, 73.2, 118.8, 126.6, 128.5, 131.0, 132.4, 138.4, 148.6, 152.7, 156.6, 160.2, 162.4; *Anal*. Calcd for $C_{20}H_{17}N_3O_5$: C, 63.32; H, 4.52; N, 11.08; found: C, 63.18; H, 4.40; N, 10.93.

***Ethyl-3-amino-5,10-dihydro-1-(4-dimethylaminophenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5n).*** Brown solid, IR ($\nu_{max}$, KBr) 3356, 3274, 2922, 2211, 1726, 1687, 1637, 1595 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.35 (t, 3H, $^3J_{HH}$ = 7.36 Hz, $CH_3$), 3.08 (s, 6H, 2 × $CH_3$), 4.31 (q, 2H, $^3J_{HH}$ = 6.6 Hz, $OCH_2$), 5.64 (s, 1H, Ar–CH), 6.57–6.69 (m, 4H, Ar–H), 7.71–7.73 (m, 2H), 7.88–7.93 (m, 2H), 8.05 (br s, 2H, $NH_2$); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 13.1, 45.4, 60.4, 69.1, 92.0, 110.3, 124.2, 128.0, 130.6, 132.0, 132.7, 140.0, 152.4, 154.3, 162.6, 163.7; *Anal*. Calcd for $C_{22}H_{22}N_4O_4$: C, 65.01; H, 5.46; N, 13.78; found: C, 64.87; H, 5.29; N, 13.52.

***Ethyl-3-amino-5,10-dihydro-1-(styryl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5o).*** Yellow solid, IR ($\nu_{max}$, nujol) 3422, 3276, 2923, 2221, 1713, 1694, 1638 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.36 (t, 3H, $^3J_{HH}$ = 7.32 Hz, $CH_3$), 4.33 (q, 2H, $^3J_{HH}$ = 7.32 Hz, $OCH_2$), 6.26 (m, 1H, Ar–CH), 6.69 (m, 1H), 6.73 (d, 1H, $J$ = 14.6 Hz), 7.29 (br s, 2H, $NH_2$), 7.41–7.60 (m, 5H, Ar–H), 7.98–8.01 (m, 2H), 8.20–8.27 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 14.1, 54.6, 62.3, 76.7, 123, 126.3, 127.4, 127.6, 127.9, 128.5, 129.1, 131.2, 134.6, 148.8, 162.3, 164.1, 165.8; *Anal*. Calcd for $C_{22}H_{19}N_3O_4$: C, 67.86; H, 4.92; N, 10.79; found: C, 67.72; H, 4.75; N, 10.66.

***Ethyl-3-amino-5,10-dihydro-1-(4-hydroxy-3-methoxyphenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5p).*** Light yellow solid, IR ($\nu_{max}$, KBr) 3426, 3364, 2897, 1710, 1662, 1635 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.39 (t, 3H, $^3J_{HH}$ = 7.30 Hz, $CH_3$), 3.98 (s, 3H, $OCH_3$), 4.38 (q, 2H, $^3J_{HH}$ = 7.30 Hz, $OCH_2$), 6.23 (s, 1H, Ar–CH), 6.99–7.53 (m, 3H, Ar–H), 7.85–7.87 (m, 2H), 8.14 (br s, 2H, $NH_2$), 8.24–8.38 (m, 2H), 9.83 (br s, 1H, OH); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 14.2, 56.1, 57.0, 62.4, 99.0, 114.9, 116.4, 119.5, 128.8, 131.8, 132.1, 136.0, 142.3, 146.8, 150.9, 162.0, 163.1, 164.8; *Anal*. Calcd for $C_{21}H_{19}N_3O_6$: C, 61.61; H, 4.68; N, 10.26; found: C, 61.48; H, 4.59; N, 10.15.

***Ethyl-3-amino-5,10-dihydro-1-(1-naphthyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5q).*** Brown solid, IR ($\nu_{max}$, nujol) 3464, 3058, 2874, 2225, 1735, 1726, 1689, 1646 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.13 (t, 3H, $^3J_{HH}$ = 8.0 Hz, $CH_3$), 4.13 (q, 2H, $^3J_{HH}$ = 7.32 Hz, $OCH_2$), 6.11 (s, 1H, Ar–CH), 7.28–7.85 (m, 7H, Ar–H), 7.95–7.98 (m, 2H), 8.04 (br s, 2H, $NH_2$), 8.12–8.22 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 13.8, 61.0, 69.9, 72.3, 122.4, 125.0, 125.4, 126.2, 126.4, 127.4, 127.6, 128.8, 132, 132.4, 132.8, 133.0, 134.6, 152.3, 161.7, 165.5, 166.0; *Anal*. Calcd for $C_{24}H_{19}N_3O_4$: C, 69.72; H, 4.63; N, 10.16; found: C, 69.60; H, 4.54; N, 10.02.

***Ethyl-3-amino-5,10-dihydro-1-(1-benzo[1,3]-dioxol-5-yl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5r).*** Yellow solid, IR ($\nu_{max}$, KBr) 3324, 3167, 2900, 2219, 1725, 1654, 1620 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.39 (t, 3H, $^3J_{HH}$ = 7.32 Hz, $CH_3$), 4.36 (q, 2H, $^3J_{HH}$ = 7.32 Hz, $OCH_2$), 6.09 (s, 2H), 6.30 (s, 1H, Ar–CH), 6.80–6.93 (m, 3H, Ar–H), 7.90–7.93 (m, 2H), 8.12 (br s, 2H, $NH_2$), 8.29–8.38 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 14.2, 55.6, 62.5, 70.4, 99.8, 109.0, 116.0, 121.0, 125.9, 129.7, 132.0, 136.8, 145.6, 148.6, 152.2, 159.7, 163.0, 168.5; *Anal*. Calcd for $C_{21}H_{17}N_3O_6$: C, 61.91; H, 4.21; N, 10.31; found: C, 61.77; H, 4.03; N, 10.20.

***Ethyl-3-amino-5,10-dihydro-1-(2-furanyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5s).*** Off white solid, IR ($\nu_{max}$, KBr) 3412, 3158, 2926, 2214, 1734, 1657, 1606 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.36 (t, 3H, $^3J_{HH}$ = 6.80 Hz, $CH_3$), 4.28 (q, 2H, $^3J_{HH}$ = 6.80 Hz, $OCH_2$), 6.24 (s, 1H, Ar–CH), 6.75–6.92 (m, 3H, Ar–H), 7.88–7.92 (m, 2H), 8.05 (br s, 2H, $NH_2$), 8.18–8.28 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 14.0, 54.6, 60.3, 74.3, 106.8, 111.3, 126.3, 128.5, 129.7, 139.3, 147.6, 149.0, 157.4, 158.5, 160.6; *Anal*. Calcd for $C_{18}H_{15}N_3O_5$: C, 61.19; H, 4.28; N, 11.89; found: C, 61.10; H, 4.16; N, 11.80.

***Ethyl-3-amino-5,10-dihydro-1-(2-thienyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5t).*** Green solid, IR ($\nu_{max}$, KBr) 3448, 3165, 2896, 2227, 1735, 1661, 1600 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, TMS) δ: 1.37 (t, 3H, $^3J_{HH}$ = 7.30 Hz, $CH_3$), 4.32 (q, 2H, $^3J_{HH}$ = 7.30 Hz, $OCH_2$), 6.17 (s, 1H, Ar–CH), 6.65–6.90 (m, 3H, Ar–H), 7.65 (br s, 2H, $NH_2$), 7.83–7.86 (m, 2H), 8.22–8.32 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 14.1, 52.8, 62.5, 74.6, 122.1, 125.7, 126.4, 127.8, 129.2, 129.8, 135.6, 148.1, 157.4, 159.6, 161.7; *Anal*. Calcd for $C_{18}H_{15}N_3O_4S$: C, 58.53; H, 4.09; N, 11.38; found: C, 58.45; H, 4.02; N, 11.24.

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