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FULL PAPER

Palladium-Catalyzed Acylations: A One-Pot Diversified Synthesis of Phthalazines, Phthalazinones and Benzoxazinones

Basuli Suchand and Gedu Satyanarayana*[a]

Dedication ((optional))

Abstract: A sequential one-pot strategy for the diversified synthesis of phthalazines, phthalazinones and benzoxazinones, was presented. This strategy proceeds via [Pd]-catalyzed acylation and nucleophilic cyclocondensation with dinucleophilic reagents. This process was based on direct coupling with simple bench-top aldehydes, without the assistance of directing group and without activating the carbonyl group. The process is highly advantageous, as, it employs simple nitrogen based nucleophiles, and non-toxic & readily accessible aldehydes as the carbonyl source. Most importantly, the strategy was applied to the one-pot synthesis of PDE-4 inhibitor.

Introduction

Heterocyclic compounds are vital and ubiquitous in nature.[1] Thus, development of efficient synthetic processes to accomplish them is indispensable. In particular, the nitrogen based heterocyclic molecules have gained an exceptional importance in medicinal chemistry. Particularly, dinitrogen containing phthalazinones have been utilized to cure various diseases, for example, hepatitis B, arrhythmia, asthma, diabetes, cardiovascular and vascular hypertension (Figure 1).[2] In addition, benzoxazinone derivatives are another important class of heterocycles that exhibit interesting physiological and pharmaceutical activities, such as, anticancer, antimalarial, antifungal, antitubercular, phytotoxic, antiviral, antifeedant, anti-HIV and antibacterial.[3] While phthalazines are a special class of heterocyclic compounds,[4] having medicinal and biological significance (Figure 1).[5]

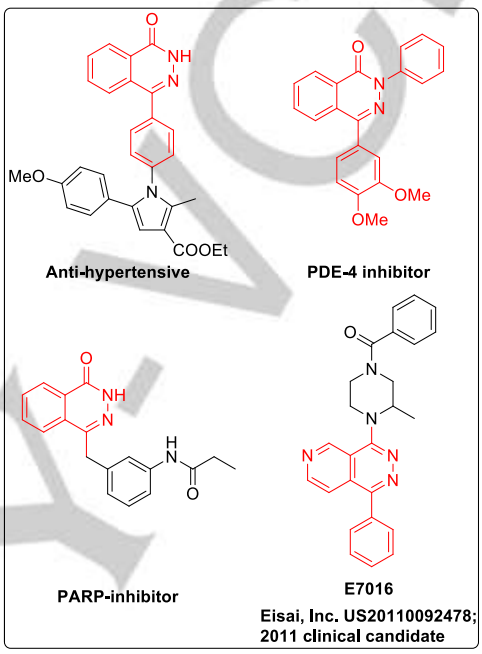

Figure 1: Representative examples of bioactive phathalazinones/phathalazine.

Owing to their interesting structural features and broad spectrum of biological activities, synthetic community has established some interesting strategies on their synthesis. In 1893, Gabriel et al first synthesized the phthalazine using substitution of 1,2-bis-dichloromethylbenzene by ring-closing reaction of *ortho*-carbonylbenzaldehyde with hydrazine.[6] Commonly, phthalazines have been achieved by using multistep procedures, such as, ring closing or ring enlargement or aromatization of 1,2-dihydro- or 1,2,4,5- tetrahydrophthalazines.[7] They were also synthesized by employing the Diels-Alder reaction of 1,2,4,5-tetrazines with arynes/arenes or pyridazino[4,5-d]pyridazine with enamines.[8] H. A. Wegner et al presented the synthesis of phthalazines and pyridazino aromatics starting from aromatic aldehydes via directed *ortho*-lithiation strategy.[9] While synthesis of phthalazinones was established by cyclocondensation and cycloaddition reactions.[10] Recently, the research group of Xiao-Feng Wu reported the carbonylative synthesis of phthalazinones from 2-bromobenzaldehydes and hydrazines, in which CO was used as the carbonylating source.[11] On the other hand, L. K. Reddy and Baburajan et al made use of $Mo(CO)_6$ and $Co_2(CO)_8$ as an alternative sources of CO, respectively.[12] Orru et al disclosed [Pd]-catalyzed isocyanide insertion to give phathalazinones,[13] while, to the best of our knowledge, there was only one report on the synthesis of benzoxazinones by

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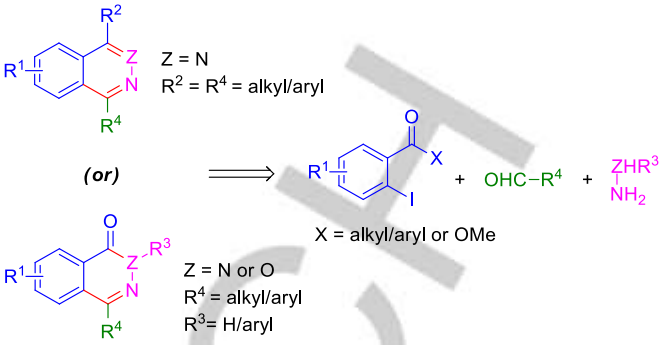
Huanfeng Jiang and co-workers via [Pd]-catalyzed carbonylation of aromatic oximes.[14]

Sequential one-pot transformations are very essential for chemical synthesis,[15] as they enable the formation of more than one bond, thereby facilitating the formation of products with sufficient complexity. Also, they are economically and ecologically viable processes, as they save time, energy and reduce amount of waste formation. Additionally, they are beneficial by reducing tedious isolation and purification steps of the intermediate product(s). Transition-metal-catalysis proved to be powerful tool for the efficient construction of C−C and C−heteroatom bonds.[16] We anticipated that a sequential one-pot synthesis of nitrogen containing heterocycles could be feasible using [Pd]-catalyzed direct acylation with aldehydes and cyclocondensation with dinucleophilic agents (Scheme 1). It was also envisaged that simple bench-top aldehydes could serve as non-toxic acyl source. As part of our ongoing research in the development of new synthetic methodologies catalyzed by transition metals,[17] very recently, [Pd]-catalyzed direct acylation of iodoarenes with aldehydes without the aid of functional group was reported by us.[18] Subsequently, we have shown the effectiveness of this concept, for a one-pot synthesis of indenones via [Pd]-catalyzed direct acylation and intramolecular aldol condensation.[19] Later, the efficacy of the concept was further proven by one-pot synthesis of lactams.[20] Encouraged by these outcomes, herein, we describe an efficient one-pot synthesis of phthalazines through [Pd]-catalyzed direct acylation of *ortho*-iodoaryl ketones with aldehydes and nucleophilic cyclocondensation with hydrazine hydrate. In addition, sequential one-pot formation of phthalazinones have been accomplished upon acylation of *ortho*-iodoaryl esters and cyclocondensation with hydrazine hydrates. Further, the synthesis of *N*-substituted phathalizinones has also been explored. Furthermore, this concept has been successfully extended to the one-pot synthesis of benzoxazinones using hydroxylamine as the nucleophile for condensation. Remarkably, this protocol enabled the one-pot synthesis of PDE-4 inhibitor.

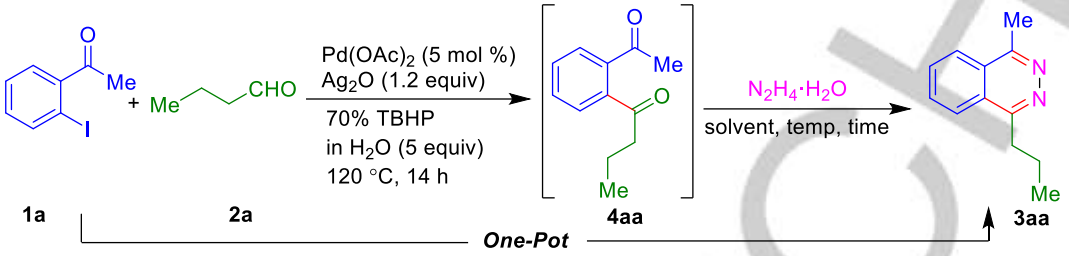


Scheme 1: Anticipated one-pot synthetic route to heterocylic products.

Results and Discussion

In order to initiate the synthetic explorations, for the preparation of phthalazine **3aa**, *ortho*-iodoacetophenone **1a** and butyraldehyde **2a**, were chosen as the model substrates. Thus, acylation was performed using our earlier established conditions [i.e. $Pd(OAc)_2$ (5 mol%), Ag_2O (1.2 equiv), TBHP in H_2O (5 equiv), 120 °C, 14 h]. After confirming the formation of diketone intermediate **4aa** by thin-layer-chromatography (TLC), the cyclocondensation with dinucleophilic hydrazine hydrate was explored, under various conditions. Addition of hydrazine hydrate to the diketone intermediate **4aa** along with the base triethylamine (2 equiv) with no additional solvent, furnished the desired phthalazine product **3aa**, in moderate yield (Table 1, entry 1). While the reaction with the base K_2CO_3 was found to be inferior (Table 1, entry 2). On the other hand, in the absence of base and solvent, the product **3aa** was obtained in poor yields (Table 1, entry 3). Slight improvement was seen with additional amount of solvent DMF in the presence of K_2CO_3 (Table 1, entry 4). More or less same yield of product **3aa** was obtained without base (Table 1, entry 5). Yield deviation was negligible even by decreasing the temperature of the reaction from 100 °C to 50 °C (Table 1, entry 6), so, there is not that much effect of high temperature. Improvement in the yield was noticed by increasing equivalents of hydrazine hydrate in DMF solvent (Table 1, entries 7). Only slight improvement was noted by using MeOH as solvent (Table 1, entry 8). Interestingly, **3aa** was obtained in 55% yield in EtOH solvent (Table 1, entries 9). Further, slight improvement of the product **3aa** was obtained with 10 equiv of hydrazine hydrate in methanol solvent (Table 1, entry 10). Upon increasing the temperature to 75 °C, yield has been improved to 62% (Table 1, entries 11). While the reaction with 10 equiv of hydrazine hydrate in ethanol at 50 °C, gave **3aa** in 64% yield (Table 1, entry 12). Gratifyingly, ethanol was found to be a better solvent than methanol and furnished the phthalazine **3aa**, in 67% overall yield, with 10 and 5 equiv of hydrazine hydrate at 75 °C, for 6 h, respectively (Table 1, entries 13 & 14). Whereas, the product **3aa** yield was decreased, when 2 equiv of hydrazine hydrate was used (Table 1, entry 15).

Table 1: Optimization study for one-pot formation of phthalazine **3aa** via the diketone **4aa**.[a]



Entry	$N_2H_4{\cdot}H_2O$ (equiv)	Base (2 equiv)	Solvent (2.0 mL)	Temp (°C)	Time (h)	Yield **3aa** (%)[b]
1.	2.0	NEt_3	-	120	6	40
2.	2.0	K_2CO_3	-	100	6	30
3	2.0	-	-	100	12	30
4	2.0	K_2CO_3	DMF	100	10	44
5	2.0	-	DMF	100	10	43
6	2.0	-	DMF	50	12	42
7	4.0	-	DMF	50	10	47
8	4.0	-	MeOH	50	15	50
9	4.0	-	EtOH	50	8	55
10	10.0	-	MeOH	50	10	58
11	10.0	-	MeOH	75	8	62
12	10.0	-	EtOH	50	8	64
13	10.0	-	EtOH	75	6	67
14	**5.0**	**-**	**EtOH**	**75**	**6**	**67**
15	2.0	-	EtOH	75	14	53

[a] Unless otherwise mentioned, all the reactions were carried out by using 98.0 mg (0.40 mmol) of *ortho*-iodoketone **1a** and aldehyde **2a (**115.0 mg, 1.6 mmol). [b] Isolated yields of chromatographically pure products.

With the established conditions in hand, [(1) for acylation: **1a** (1.0 equiv), **2a** (4.0 equiv), $Pd(OAc)_2$ (5 mol %)/Ag_2O (1.2 equiv), aqueous TBHP (5.0 equiv) at 120 °C for 14 h; (2) for nucleophilic cylcocondensation: hydrazine hydrate (5 equiv), EtOH (2 mL), 75 °C, for 6 h (Table 1, entry 13)], to check the scope and limitations for the one-pot formation of phthalizine **3aa**, the acylation and in-situ nucleophilic cyclocondensation was explored. Thus, after confirming the formation of acylation product upon coupling of *ortho*-iodoarylketones **1a-1e** with aldehydes **2a-2n**, the hydrazine hydrate and ethanol were added to the reaction mixture, under the established conditions. Delightfully, the reaction was found to be smooth and quite successful with very good substrate scope, and furnished a diversified phthalazine products **3aa-3ef** (Table 2). For example, *ortho*-iodoacetophenone **1a** coupling with aliphatic aldehydes **2a-2c** and subsequent cyclocondensation was amenable, and delivered the products **3aa-3ac** (Table 2). Notably, the one-pot reaction of **1a** and **1b** was also compatible with benzaldehydes **2e**, **2k-2m** bearing simple to electron rich aromatic ring (Table 2, **3al-3bk**). Further, *ortho*-iodobenzophenones **1c-1e**, were also smoothly transformed into the corresponding products, under standard reaction conditions (Table 2, **3cn-3ef**). Significantly, the reaction was amenable with heteroaromatic systems (Table 2, **3cn** & **3ef**). Notably, the strategy was also compatible with bromobenzaldehyde **2j** and thus would permit further functionalizations, under transition metal catalysis (Table 2, **3dj**).

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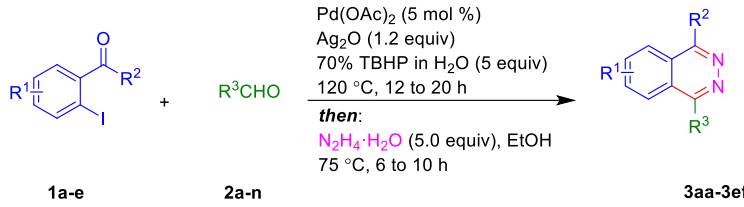
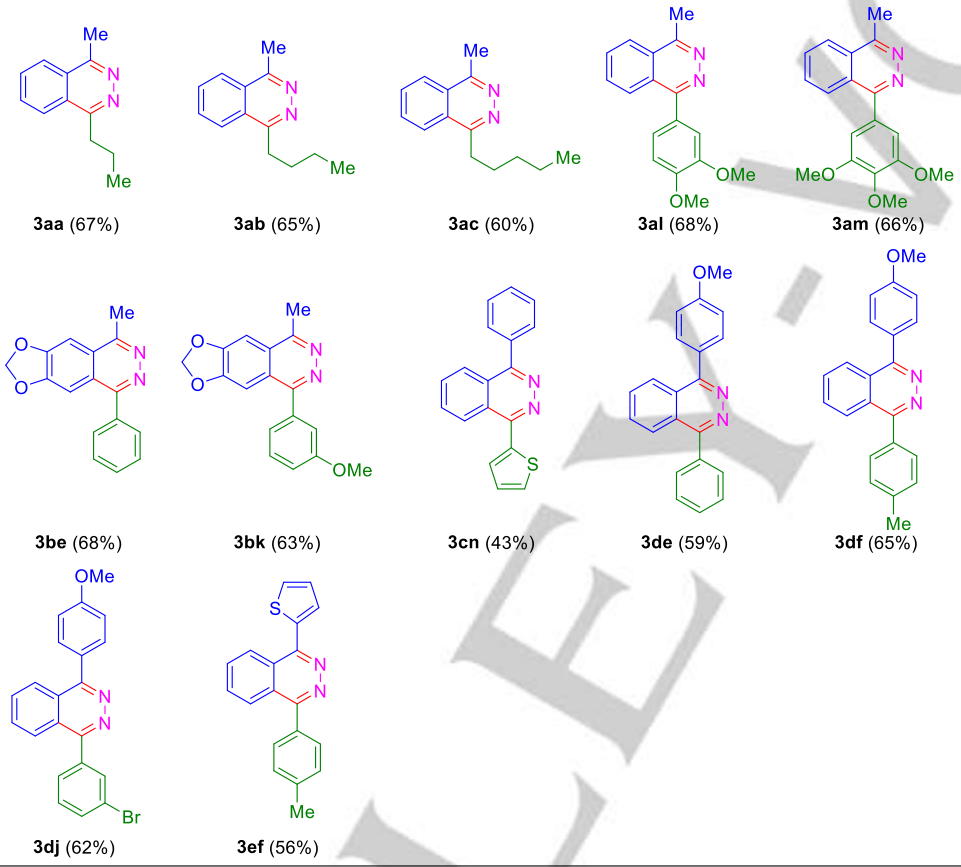
Table 2: Scope of the synthetic study for one-pot synthesis of phthalazines **3aa-3ef**.[a]



1a-e **2a-n** **3aa-3ef**



3aa (67%) **3ab** (65%) **3ac** (60%) **3al** (68%) **3am** (66%)

3be (68%) **3bk** (63%) **3cn** (43%) **3de** (59%) **3df** (65%)

3dj (62%) **3ef** (56%)

[a] Isolated yields of chromatographically pure products.

Further, to emphasize the importance of the present method, it was aimed at the one-pot synthesis of phthalazinones. For this purpose, *ortho*-iodobenzoate **1f** was identified as the suitable starting material. Thus, acylation of *ortho*-iodomethylbenzoate **1f** with aliphatic aldehydes **2a-2d** and subsequent condensation with nitrogen based nucleophlies was carried out, under the established conditions. Gratifyingly, the desired phthalazinones **5fa-5fd** were obtained as the exclusive products (Table 3). In addition, the reaction was also smooth with benzaldehydes **2e-2i**, **2l** ranging from simple, electron rich and electron deactivating aromatic rings (Table 3, **5fe-5fl**), thus, emphasizing the importance of the present protocol.

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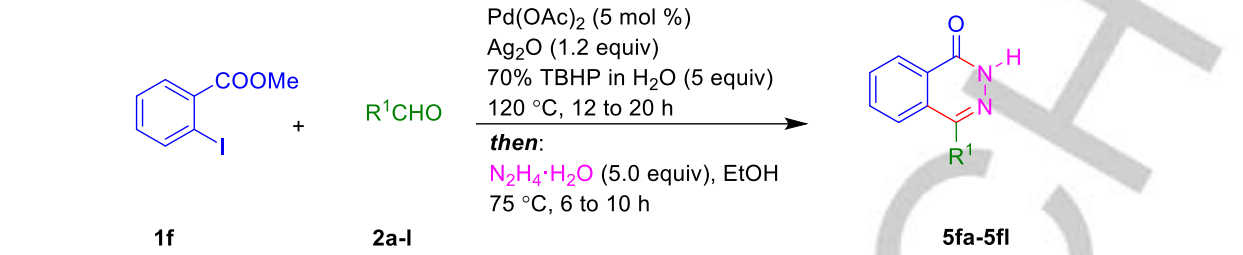
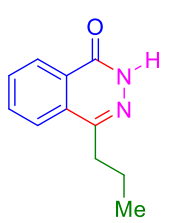
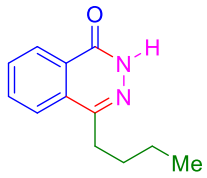
Table 3: One-pot synthesis of phthalazinones **5fa-5fl**. [a]



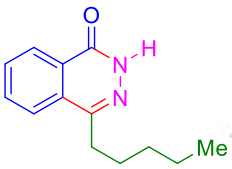
1f **2a-l** **5fa-5fl**



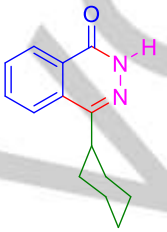
5fa (64%)



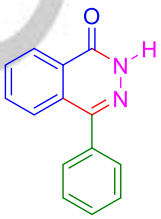
5fb (65%)



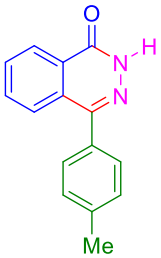
5fc (62%)



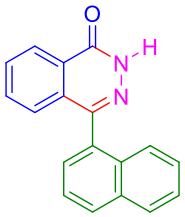
5fd (68%)



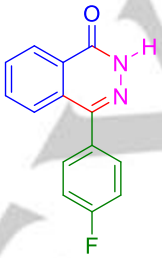
5fe (71%)



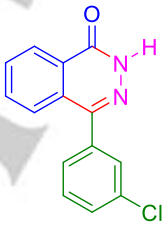
5ff (63%)



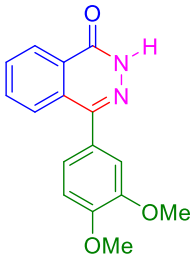
5fg (63%)



5fh (57%)



5fi (60%)



5fl (72%)

[a] Isolated yields of chromatographically pure products.

Further, to demonstrate the synthetic utility of the present strategy, it was planned for the one-pot synthesis of *N*-substituted phthalazinones. This could be achieved upon subjecting the acylated dicarbonyl intermediate to *N*-protected hydrazine hydrochloride analogs **8**. Thus, after monitoring the formation of ketone intermediate by TLC, the reaction mixture was treated with different hydrazine analogs **8a**-**8e**, to drive subsequent cyclocondensation. To our delight, as anticipated, the strategy was smooth with aliphatic aldehydes **2a**-**2c**, under stablished conditions (Table 4, **6faa**-**6fbe**). However, the reaction was sluggish when aromatic aldehydes were employed as the acylating agents. This may be due to the fact that *N*-arylated hydrazines are somewhat less nucleophilic than that of simple hydrazine hydrate. Moreover, the corresponding ketone intermediate generated from aromatic aldehydes is less electrophilic than aliphatic ones. Hence, it is necessary to optimize the conditions, for the formation of corresponding *N*-substituted phthalazinones with aromatic aldehydes. After exploring the reaction under different conditions, it was realized that conc. H_2SO_4 (10 equiv), as an additive was best to drive the cyclocondensation step. Further, these modified optimized conditions enable the synthesis of *N*-substituted phthalazinones (Table 4, **6fea**-**6fhe**).

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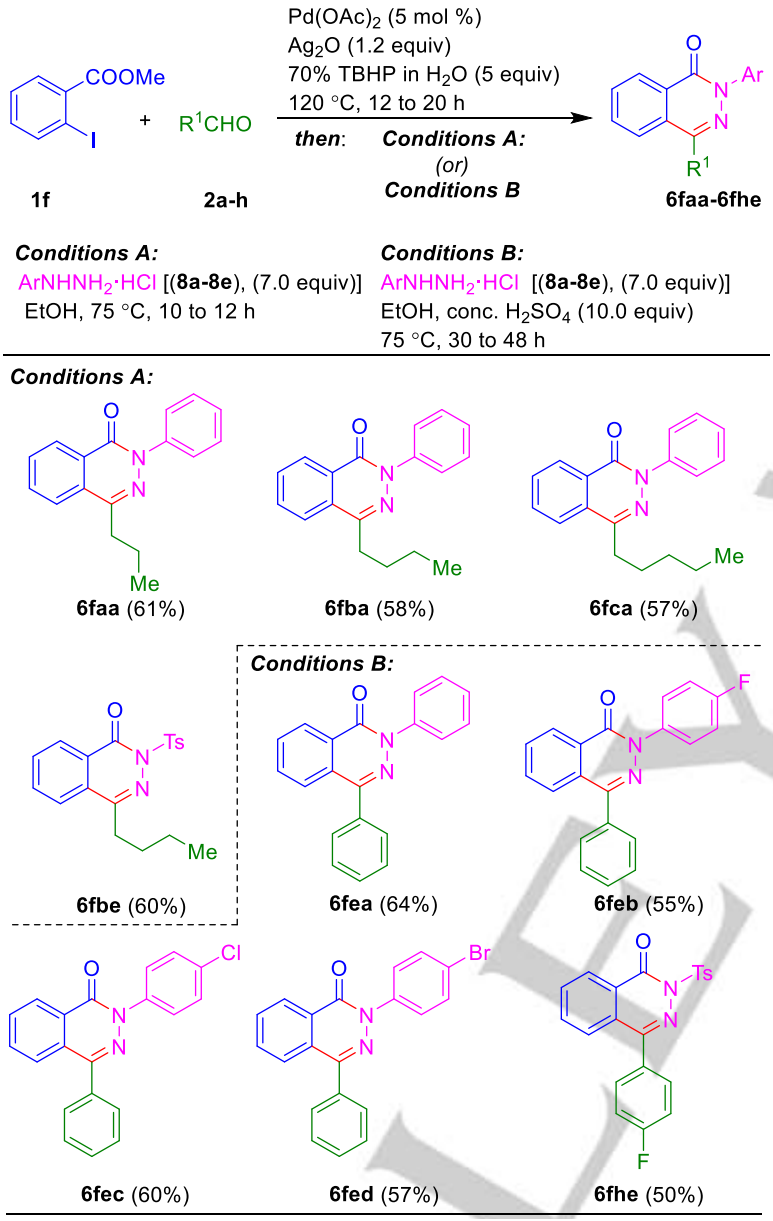
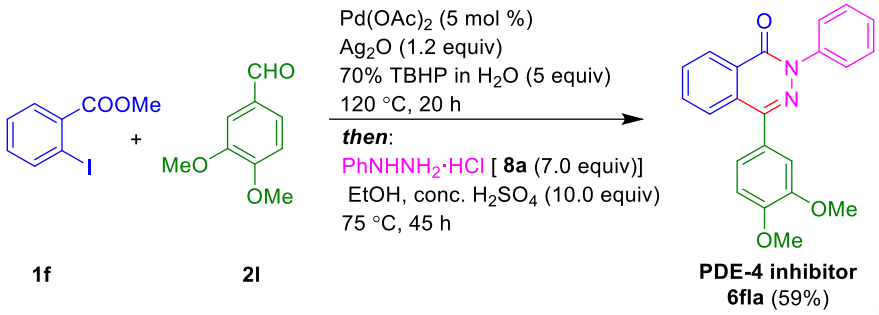
Table 4: One-pot synthesis of *N*-substituted phthalazinones **6faa-6fhe**. [a]



[a] Isolated yields of chromatographically pure products.

Furthermore, to reveal the importance of present method, it was aimed at the one-pot synthesis of PDE-4 inhibitor. Thus, *ortho*-iodomethylbenzoate **1f** was subjected to acylation with veratraldehyde **2l** and subsequent condensation with phenylhydrazine hydrochloride **8a** (Scheme 2). Gratifyingly, the target product PDE-4 inhibitor **6fla** was obtained in 59% overall yield.

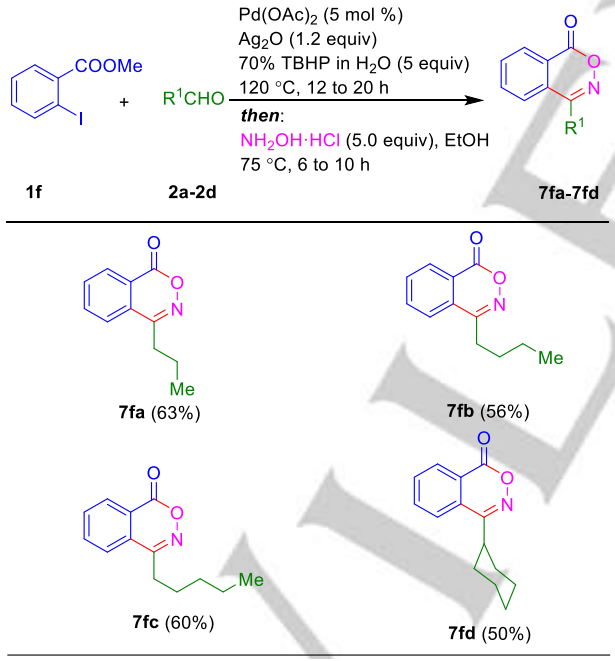


1f **2l** **PDE-4 inhibitor 6fla** (59%)

Scheme 2: One-pot synthesis of PDE-4 inhibitor **6fla**.

Moreover, to establish the diversity of this protocol, one-pot synthesis of benzoxazinones was aimed. Thus, in-situ formed ketones were reacted with hydroxylamine hydrochloride. Delightfully, as presumed, the benzoxazinones **7fa-7fd** were accomplished, in moderate to fair yields (Table 5). It is worth mentioning that the reaction was sluggish when attempts were made with aromatic aldehydes as acylating agents. This could be due to less nucleophilic nature of hydroxylamine hydrochloride. In addition, the acylated aromatic ketones are slightly less reactive than aliphatic ones.

Table 5: One-pot synthesis of benzoxazinones **7fa-7fd**. [a]



1f **2a-2d** **7fa-7fd**

7fa (63%) **7fb** (56%) **7fc** (60%) **7fd** (50%)

[a] Isolated yields of chromatographically pure products.

Conclusions

In summary, a sequential one-pot method was developed for the efficient and diversified synthesis of phthalazines, phthalazinones and benzoxazinones. The whole process proceeds through [Pd]-catalyzed intermolecular acylation and nucleophilic condensation with dinucleophiles. Simple bench-top aldehydes and nitrogen based nucleophiles were employed, as non-toxic sources. This process was relied upon direct coupling with aldehydes, without the activation of the carbonyl group and no directing group assistance is needed. Significantly, the effectiveness of strategy has been established by one-pot synthesis of PDE-4 inhibitor.

Experimental Section

IR spectra were recorded on a FTIR spectrophotometer. ^{1}H NMR spectra were recorded on 400 MHz spectrometer at 295 K in $CDCl_3$; chemical shifts (δ ppm) and coupling constants (Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) (δ_H =0.00 ppm) or $CHCl_3$ (δ_H = 7.25 ppm). ^{13}C NMR spectra were recorded on 100 MHz spectrometer at RT in $CDCl_3$; chemical shifts (δ ppm) are reported relative to $CHCl_3$ [δ_C = 77.00 ppm (central line of triplet)]. In the ^{13}C NMR, the nature of carbons (C, CH, CH_2 and CH_3) was determined by recording the DEPT-135 spectra. In the ^{1}H-NMR, the following abbreviations were used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui =quintet, sept = septet, dd = doublet of doublet, m = multiplet and br. s = broad singlet. High-resolution mass spectra (HR-MS) were recorded on Q-TOF electron spray ionization (ESI) mode and atmospheric pressure chemical ionization (APCI) modes. Melting points were determined on an electrothermal melting point apparatus and are uncorrected.

All small scale reactions were carried out using Schlenk tube. Reactions were monitored by TLC on silica gel using a combination of hexane and ethyl acetate as eluents. Reactions were generally run under argon or a nitrogen atmosphere. Solvents were distilled prior to use; petroleum ether with a boiling range of 60 to 80 °C was used. Acme's silica-gel (60–120 mesh) was used for column chromatography (approximately 20 g per one gram of crude material).

The aldehydes **2a-n** which have been used are commercially available. The *ortho*-iodoester **1f** is commercially available.

The following *ortho*-iodo ketone **1a-e** was synthesized from **10a-d** which is reported (Table 6, see supporting information).

GP-1 [General procedure for preparation of 3/5]:

GP-1 was carried out with *ortho*-iodoketone/*ortho*-iodoester **1a-f** (98.0-135.0 mg, 0.40 mmol**)** and aldehyde **2a-n (**115.0-313.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 12-20 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone/ *ortho*-iodoester **1a-f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 6-10 h. Progress of the products **3/5** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3/5** (50.0-106.0 mg, 43-72 %). The products **3al**, **3am**, **3de** and **5fa-5fl** are reported in literature.[21]

GP-2 [General procedure (condition A) for preparation of 6faa-6fbe]:

GP-2 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2a-c** (115.0-160.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 12-18 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and *N*-protected hydrazine hydrochloride **8** (410.0-623.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 10-12 h. Progress of the products **6** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6faa-6fbe** (65.0-106.0 mg, 57-61 %).

GP-3 [General procedure (condition B) for preparation of 6fea-6fhe]:

GP-3 was f carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2e-h (**169.0-198.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 12-20 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml), conc. H_2SO_4 (0.39 ml, 4.0 mmol) and *N*-protected hydrazine hydrochloride **8** (410.0-623.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 40-48 h. Progress of the products **6** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6fea-6fhe** (67.0-86.0 mg, 50-64 %). The products **6fea**, **6feb**, **6fec**, **6fed** are reported in literature.[22, 12b]

GP-4 [General procedure for preparation of 7]:

GP-4 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2a-d** (115.0-179.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 12-20 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydroxylamine hydrochloride (138.0 mg, 2.0 mmol) and allowed the reaction mixture stirred at 75 °C for 6-10 h. Progress of the products **7** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **7** (46.0-52.0 mg, 50-63 %). The products **7fa** are reported in literature.[14]

1-methyl-4-propylphthalazine (**3aa**): GP-1 was carried out with *ortho*-iodoketone **1a** (98.0 mg, 0.40 mmol**)** and aldehyde **2a (**115.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1a** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 6 h. Progress of the products **3aa** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3aa** (50.0 mg, 67 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.80, R_f(**3aa**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2938, 1710, 1682, 1594, 1452, 1282, 1081, 904, 728 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.09-8.03 (m, 2H, Ar-H), 7.86-7.84 (m, 2H, Ar-H), 3.29-3.25 (m, 2H), 2.94 (s, 3H, CH_3), 1.92-1.86 (m, 2H), 1.05 (t, J = 7.3 Hz, 3H, CH_3), ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=159.4 (s, Ar-C=N), 156.1 (s, Ar-C=N), 131.7 (d, Ar-CH), 131.6 (d, Ar-CH), 126.2 (s, Ar-C), 125.3 (s, Ar-C), 124.9 (d, Ar-CH), 124.5 (d, Ar-CH), 34.9 (t, –CH_2–), 22.7 (t, –CH_2–), 19.7 (q, *C*H3), 14.2 (q, *C*H3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{12}H_{15}N_2]^+$=$[M+H]^+$: 187.1230; found 187.1236.

1-butyl-4-methylphthalazine (**3ab**): GP-1 was carried out with *ortho*-iodoketone **1a** (98.0 mg, 0.40 mmol**)** and aldehyde **2b** (137.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 12 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1a** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **3ab** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution,

dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3ab** (52.0 mg, 65 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.80, R_f(**3aa**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2936, 1720, 1684, 1590, 1451, 1280, 1189, 943, 705 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.08-8.02 (m, 2H, Ar-H), 7.86-7.83 (m, 2H, Ar-H), 3.30-3.27 (m, 2H), 2.93 (s, 3H, CH_3), 1.87-1.79 (m, 2H), 1.52-1.43 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H, CH_3), ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=159.6 (s, Ar-C=N), 156.0 (s, Ar-C=N), 131.6 (d, Ar-CH), 131.5 (d, Ar-CH), 126.1 (s, Ar-C), 125.2 (s, Ar-C), 124.9 (d, Ar-CH), 124.5 (d, Ar-CH), 32.8 (t, –CH_2–), 31.5 (t, –CH_2–), 22.8 (t, –CH_2–), 19.7 (q, *C*H3), 13.9 (q, *C*H_3) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{13}H_{17}N_2]^+$=$[M+H]^+$: 201.1386; found 201.1382.

1-methyl-4-pentylphthalazine (**3ac**): GP-1 was carried out with *ortho*-iodoketone **1a** (98.0 mg, 0.40 mmol**)** and aldehyde **2c** (160.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 15 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1b** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **3ac** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3ac** (51.0 mg, 60 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.80, R_f(**3ac**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2938, 1719, 1687, 1612, 1460, 1280, 1081, 914, 705 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.09-8.03 (m, 2H, Ar-H), 7.86-7.84 (m, 2H, Ar-H), 3.30-3.26 (m, 2H), 2.94 (s, 3H, CH_3), 1.89-1.81 (m, 2H), 1.46-1.33 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H, CH_3), ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=159.6 (s, Ar-C=N), 156.0 (s, Ar-C=N), 131.6 (d, Ar-CH), 131.5 (d, Ar-CH), 126.2 (s, Ar-C), 125.2 (s, Ar-C), 124.9 (d, Ar-CH), 124.5 (d, Ar-CH), 33.1 (t, –CH_2–), 31.8 (t, –CH_2–), 29.1 (t, –CH_2–), 22.5 (t, –CH_2–), 19.7 (q, *C*H3), 13.9 (q, *C*H3) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{14}H_{19}N_2]^+$=$[M+H]^+$: 215.1543; found 215.1537.

1-(3,4-dimethoxyphenyl)-4-methylphthalazine (**3al**): GP-1 was carried out with *ortho*-iodoketone **1a** (98.0 mg, 0.40 mmol**)** and aldehyde **2l (**265.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 20 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1a** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 10 h. Progress of the products **3al** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3al** (76.0 mg, 68 %).

1-methyl-4-(3,4,5-trimethoxyphenyl)phthalazine (**3am**): GP-1 was carried out with *ortho*-iodoketone **1a** (98.0 mg, 0.40 mmol**)** and aldehyde **2m (**314.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 20 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1a** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **3am** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3am** (82.0 mg, 66 %).

5-methyl-8-phenyl-[1,3]dioxolo[4,5-g]phthalazine (**3be**): GP-1 was carried out with *ortho*-iodoketone **1b** (116.0 mg, 0.40 mmol**)** and aldehyde **2e (**169.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 18 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1b** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 10 h. Progress of the products **3be** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3be** (106.0 mg, 68 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.80, R_f(**3be**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2930, 1705, 1680, 1595, 1453, 1283, 1085, 912, 705 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.63-7.61 (m, 2H, Ar-H), 7.50-7.49 (m, 3H, Ar-H), 7.31 (s, 1H, Ar-H), 7.22 (s, 1H, Ar-H), 6.13 (s, 2H, -OCH_2O-), 2.91 (s, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=158.1 (s, Ar-C=N), 155.1 (s, Ar-C=N), 151.4 (s, 2 × Ar-C), 136.6 (s, Ar-C), 129.7 (d, 2 × Ar–CH), 128.9 (d, Ar-CH), 128.4 (d, 2 × Ar–CH), 124.7 (s, Ar-C), 123.3 (s, Ar-C), 103.1 (d, Ar–CH), 102.3 (t, –CH_2–), 101.1 (d, Ar–CH), 20.0 (q, *C*H_3) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{16}H_{13}N_2O_2]^+$=$[M+H]^+$: 265.0972; found 265.0973.

5-(3-methoxyphenyl)-8-methyl-[1,3]dioxolo[4,5-g]phthalazine (**3bk**): GP-1 was carried out with *ortho*-iodoketone **1b** (116.0 mg, 0.40 mmol**)** and aldehyde **2k (**218.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 15 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1b** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 7 h. Progress of the products **3bk** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$

solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3bk** (74.0 mg, 63 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.80, R_f(**3bk**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2932, 1719, 1676, 1590, 1451, 1280, 1189, 914, 708 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ= 7.40 (t, J = 7.8 Hz, 1H, Ar-H), 7.29 (s, 1H, Ar-H), 7.25 (s, 1H, Ar-H), 7.19-7.16 (m, 2H, Ar-H), 7.01 (dd, J = 8.3 Hz and 2.4 Hz, 1H, Ar-H), 6.12 (s, 2H, -OCH_2O-), 3.83 (s, 3H, -OCH_3), 2.90 (s, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=159.6 (s, 2 × Ar-C), 158.0 (s, Ar-C=N), 155.2 (s, Ar-C=N), 151.3 (s, 2 × Ar-C), 138.0 (s, Ar-C), 129.4 (d, Ar–CH), 124.7 (s, Ar-C), 123.2 (s, Ar-C), 122.1 (d, Ar–CH), 115.0 (d, Ar–CH), 115.0 (d, Ar–CH), 103.1 (d, Ar–CH), 102.3 (t, –CH_2–), 101.1 (d, Ar–CH), 55.3 (q, *C*H_3), 20.1 (q, *C*H_3) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{17}H_{15}N_2O_3]^+$=[M+H]$^+$: 295.1077; found 295.1070.

1-phenyl-4-(thiophen-2-yl)phthalazine (**3cn**): GP-1 was carried out with *ortho*-iodoketone **1c** (123.0 mg, 0.40 mmol**)** and aldehyde **2n** (179.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 18 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1c** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **3cn** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3cn** (46.0 mg, 43 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.80, R_f(**3cn**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2943, 1713, 1689, 1590, 1451, 1287, 1189, 923, 711 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.55 (d, J = 8.8 Hz, 1H, Ar-H), 8.13 (d, J = 8.8 Hz, 1H, Ar-H), 7.94-7.83 (m, 2H, Ar-H), 7.80-7.77 (m, 2H, Ar-H), 7.73-7.72 (m, 1H, Ar-H), 7.61-7.54 (m, 4H, Ar-H), 7.27-7.25 (m, 1H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=158.6 (s, Ar-C=N), 152.8 (s, Ar-C=N), 139.0 (s, Ar-C), 136.2 (s, Ar-C), 132.3 (d, Ar-CH), 132.0 (d, Ar–CH), 130.2 (d, 2 × Ar–CH), 129.7 (d, Ar–CH), 129.3 (d, Ar–CH), 129.0 (d, Ar–CH), 128.5 (d, 2 × Ar–CH), 127.6 (d, Ar–CH), 126.8 (d, Ar–CH), 125.9 (s, Ar-C), 125.8 (d, Ar-CH), 125.2 (s, Ar-C) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{18}H_{13}N_2S]^+$=[M+H]$^+$: 289.0794; found 289.0790.

1-(4-methoxyphenyl)-4-phenylphthalazine (**3de**): GP-1 was carried out with *ortho*-iodoketone **1d** (135.0 mg, 0.40 mmol**)** and aldehyde **2e** (169.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 16 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1d** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 10 h. Progress of the products **3de** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3de** (74.0 mg, 59 %).

1-(4-methoxyphenyl)-4-(p-tolyl)phthalazine (**3df**): GP-1 was carried out with *ortho*-iodoketone **1d** (135.0 mg, 0.40 mmol**)** and aldehyde **2f** (192.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 15 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1d** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **3df** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3df** (85.0 mg, 65 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.80, R_f(**3df**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2938, 1720, 1685, 1509, 1455, 1286, 1087, 935, 730 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.17-8.13 (m, 2H, Ar-H), 7.83-7.81 (m, 2H, Ar-H), 7.78-7.76 (m, 2H, Ar-H), 7.69 (d, J = 8.3 Hz, 2H, Ar-H), 7.38 (d, J = 7.8 Hz, 2H, Ar-H), 7.10 (d, J = 8.8 Hz, 2H, Ar-H), 3.91 (s, 3H, -OCH_3), 2.48 (s, 3H, Ar-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=160.5 (s, Ar-C), 158.7 (s, Ar-C=N), 158.4 (s, Ar-C=N), 139.2 (s, Ar-C), 133.5 (s, Ar-C), 131.7 (d, Ar-CH), 131.6 (d, 2 × Ar–CH), 130.1 (d, 2 × Ar–CH), 129.2 (d, 2 × Ar–CH), 128.8 (s, Ar-C), 126.6 (d, Ar-CH), 126.5 (d, Ar-CH), 126.0 (s, Ar-C), 125.9 (s, Ar-C), 114.0 (d, 2 × Ar–CH), 55.4 (q, *C*H3), 21.4 (q, *C*H3) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{22}H_{19}N_2O]^+$=[M+H]$^+$: 327.1492; found 327.1490.

1-(3-bromophenyl)-4-(4-methoxyphenyl)phthalazine (**3dj**): GP-1 was carried out with *ortho*-iodoketone **1d** (135.0 mg, 0.40 mmol**)** and aldehyde **2j (**115.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 20 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1d** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **3dj** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3dj** (97.0 mg, 62 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.80, R_f(**3dj**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2940, 1705, 1687, 1589, 1451, 1287, 1182, 904, 728 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.21-8.11 (m, 1H, Ar-H), 8.08-8.04 (m, 1H, Ar-H), 7.95 (t, J = 1.7 Hz, 1H, Ar-H), 7.88-7.85 (m, 2H, Ar-H), 7.78-7.67 (m, 4H, Ar-H), 7.45 (t, J = 7.8 Hz, 1H, Ar-H), 7.11 (d, J = 8.8 Hz, 2H, Ar-H), 3.91 (s, 3H, -OCH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=160.7 (s, Ar-C), 159.0 (s, Ar-C=N), 157.3 (s, Ar-C=N), 138.4 (s, Ar-C), 133.0 (d, Ar-CH), 132.3 (d, Ar–CH), 132.1 (d, Ar–CH), 132.0 (d, Ar–CH), 131.6 (d, 2 × Ar–CH), 130.0 (d, Ar–CH), 128.7 (d, Ar–CH), 128.5 (s,

Ar-C), 126.8 (d, Ar-CH), 126.0 (d, Ar-CH), 125.8 (s, Ar-C), 125.7 (s, Ar-C), 122.6 (s, Ar-C), 114.1 (d, 2 × Ar–CH), 55.4 (q, *C*H3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{21}H_{16}BrN_2O]^+=[M+H]^+$: 391.0441; found 391.0445.

1-(thiophen-2-yl)-4-(p-tolyl)phthalazine (**3ef**): GP-1 was carried out with *ortho*-iodoketone **1e** (125.0 mg, 0.40 mmol**)** and aldehyde **2f** (192.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 18 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1e** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 9 h. Progress of the products **3ef** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3ef** (68.0 mg, 56 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.80, R_f(**3ef**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3003, 1709, 1679, 1632, 1534, 1451, 1283, 1089, 924, 719 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=8.53 (d, *J* = 7.8 Hz, 1H, Ar-H), 8.17-8.15 (m, 1H, Ar-H), 7.93-7.83 (m, 2H, Ar-H), 7.73-7.69 (m, 3H, Ar-H), 7.59 (dd, *J* = 4.8 Hz and 0.9 Hz , 1H, Ar-H), 7.38 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.26 (dd, *J* = 4.8 Hz and 3.9 Hz , 1H, Ar-H), 2.48 (s, 3H, Ar-CH_3 ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=158.5 (s, Ar-C=N), 152.6 (s, Ar-C=N), 139.3 (s, Ar-C), 139.0 (s, Ar-C), 133.3 (s, Ar-C), 132.2 (d, Ar-CH), 131.9 (d, Ar–CH), 130.1 (d, 2 × Ar–CH), 129.6 (d, Ar–CH), 129.2 (d, 2 × Ar–CH), 128.8 (d, Ar–CH), 127.6 (d, Ar–CH), 126.8 (d, Ar–CH), 125.8 (s, Ar-C), 125.7 (d, Ar-CH), 125.2 (s, Ar-C), 21.4 (q, *C*H3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{19}H_{14}N_2NaS]^+=[M+Na]^+$: 325.0770; found 325.0773.

4-propylphthalazin-1(2H)-one (**5fa**): GP-1 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2a** (115.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 6 h. Progress of the products **5fa** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5fa** (48.0 mg, 64 %). [TLC control (petroleum ether/ethyl acetate 50:50), R_f(**1f**)=1.0, R_f(**5fa**)=0.30, UV detection].

4-butylphthalazin-1(2H)-one (**5fb**): GP-1 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2b** (137.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 12 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 6 h. Progress of the products **5fb** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5fb** (52.0 mg, 65 %). [TLC control (petroleum ether/ethyl acetate 50:50), R_f(**1f**)=1.0, R_f(**5fb**)=0.30, UV detection].

4-pentylphthalazin-1(2H)-one (**5fc**): GP-1 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2c** (160.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 6 h. Progress of the products **5fc** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5fc** (64.0 mg, 62 %). [TLC control (petroleum ether/ethyl acetate 50:50), R_f(**1f**)=1.0, R_f(**5fc**)=0.30, UV detection].

4-cyclohexylphthalazin-1(2H)-one (**5fd**): GP-1 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol) and aldehyde **2d** (179.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 13 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 7 h. Progress of the products **5fc** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5fd** (91.2 mg, 68 %).[TLC control (petroleum ether/ethyl acetate 50:50), R_f(**1f**)=1.0, R_f(**5fc**)=0.30, UV detection].

4-phenylphthalazin-1(2H)-one (**5fe**): GP-1 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol) and aldehyde **2e** (169.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 6 h. Progress of the products **5fe** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5fe** (63.0 mg, 71 %). [TLC control (petroleum ether/ethyl acetate 20:80), R_f(**1f**)=1.0, R_f(**5fe**)=0.30, UV detection].

4-(p-tolyl)phthalazin-1(2H)-one (**5ff**): GP-1 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol) and aldehyde **2f** (192.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 19 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **5ff** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5ff** (60.0 mg, 63 %). [TLC control (petroleum ether/ethyl acetate 20:80), R_f(**1f**)=1.0, R_f(**5ff**)=0.30, UV detection].

4-(naphthalen-1-yl)phthalazin-1(2H)-one (**5fg**): GP-1 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol) and aldehyde **2g** (249.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 17 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 9 h. Progress of the products **5fg** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5fg** (69.0 mg, 63 %).[TLC control (petroleum ether/ethyl acetate 20:80), R_f(**1f**)=1.0, R_f(**5fg**)=0.30, UV detection].

4-(4-fluorophenyl)phthalazin-1(2H)-one (**5fh**): GP-1 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol) and aldehyde **2h** (198.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 18 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 6 h. Progress of the products **5fh** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5fh** (55.0 mg, 57 %). [TLC control (petroleum ether/ethyl acetate 20:80), R_f(**1f**)=1.0, R_f(**5fh**)=0.30, UV detection].

4-(3-chlorophenyl)phthalazin-1(2H)-one (**5fi**): GP-1 was carried out with *ortho*- iodoester **1f** (105.0 mg, 0.40 mmol) and aldehyde **2i** (224.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 17 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 9 h. Progress of the products **5fi** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5fi** (102.0 mg, 60 %). [TLC control (petroleum ether/ethyl acetate 20:80), R_f(**1f**)=1.0, R_f(**5fi**)=0.30, UV detection].

4-(3,4-dimethoxyphenyl)phthalazin-1(2H)-one (**5fl**): GP-1 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol) and aldehyde **2l** (265.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 20 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydrazine mono hydrate (99.0 mg, 1.99 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **5fl** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5fl** (81.0 mg, 72 %).[TLC control (petroleum ether/ethyl acetate 20:80), R_f(**1f**)=1.0, R_f(**5fl**)=0.20, UV detection].

2-phenyl-4-propylphthalazin-1(2H)-one (**6faa**): GP-1 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2a** (115.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and *N*-protected hydrazine

hydrochloride **8a** (410.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **6faa** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6faa** (106.0 mg, 61 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**6faa**)=0.50, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3030, 1719, 1678, 1595, 1451, 1283, 1182, 914, 718, 675 cm^{-1}.^{1}H NMR ($CDCl_3$, 400 MHz): δ= 8.54 (d, J = 7.8 Hz, 1H, Ar-H), 7.84-7.77 (m, 3H, Ar-H), 7.70-7.68 (m, 2H, Ar-H), 7.48 (t, J = 7.8 Hz, 2H, Ar-H), 7.37-7.33 (m, 3H, Ar-H), 2.99-2.95 (m, 2H), 1.89-1.79 (m, 2H), 1.06 (t, J = 7.3 Hz, 3H, CH_3), ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=159.0 (s, C=O), 147.1 (s, Ar-C=N), 142.0 (s, Ar-C), 133.1 (d, Ar-CH), 131.3 (d, Ar-CH), 129.1 (s, Ar-C), 128.6 (d, 2 × Ar-CH), 128.6 (s, Ar-C), 127.7 (d, Ar-CH), 127.4 (d, Ar-CH), 125.6 (d, 2 × Ar-CH), 124.5 (d, Ar-CH), 34.2 (t, –CH_2–), 21.4 (t, –CH_2–), 13.9 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{17}H_{17}N_2O]^+$=$[M+H]^+$: 265.1335; found 265.1331.

4-butyl-2-phenylphthalazin-1(2H)-one (**6fba**): GP-1 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2b** (137.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and *N*-protected hydrazine hydrochloride **8a** (410.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 6 h. Progress of the products **6fba** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6fba** (64.0 mg, 58 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**6fba**)=0.50, UV detection].

4-pentyl-2-phenylphthalazin-1(2H)-one (**6fca**): GP-2 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2c** (160.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and *N*-protected hydrazine hydrochloride **8a** (410.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 10 h. Progress of the products **6fca** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6fca** (67.0 mg, 57 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**6fca**)=0.50, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3012, 1704, 1685, 1593, 1453, 1284, 1189, 914, 700 cm^{-1}.^{1}H NMR ($CDCl_3$, 400 MHz): δ= 8.54 (dd, J = 7.5 Hz and 1.2 Hz, 1H, Ar-H), 7.84-7.82 (m, 2H, Ar-H), 7.79-7.76 (m, 1H, Ar-H), 7.68 (dd, J = 7.5 Hz and 1.2 Hz, 2H, Ar-H), 7.50-7.46 (m, 2H, Ar-H), 7.38-7.33 (m, 2H, Ar-H), 3.01-2.97 (m, 2H), 1.84-1.77 (m, 2H), 1.47-1.35 (m, 4H), 0.91 (t, J = 7.3 Hz, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=159.0 (s, C=O), 147.4 (s, Ar-C=N), 142.0 (s, Ar-C), 133.1 (d, Ar-CH), 131.3 (d, Ar-CH), 129.1 (s, Ar-C), 128.6 (d, 2 × Ar-CH), 128.6 (s, Ar-C), 127.7 (d, Ar-CH), 127.4 (d, Ar-CH), 125.7 (d, 2 × Ar-CH), 124.5 (d, Ar-CH), 32.3 (t, –CH_2–), 31.6 (t, –CH_2–), 27.8 (t, –CH_2–), 22.4 (t, –CH_2–), 14.0 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{19}H_{21}N_2O]^+$=$[M+H]^+$: 293.1648; found 293.1643.

4-butyl-2-tosylphthalazin-1(2H)-one (**6fbe**): GP-2 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2b** (137.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and *N*-protected hydrazine hydrochloride **8e** (623.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 10 h. Progress of the products **6fbe** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6fbe** (86.0 mg, 60 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**6fbe**)=0.50, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3010, 1700, 1682, 1509, 1451, 1285, 1084, 938, 716 cm^{-1}.^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.35-8.32 (m, 1H, Ar-H), 8.08 (d, J = 8.3 Hz, 2H, Ar-H), 7.84-7.80 (m, 1H, Ar-H), 7.77-7.75 (m, 1H, Ar-H), 7.72-7.68 (m, 1H, Ar-H), 7.33 (d, J = 7.8 Hz, 2H, Ar-H), 3.00-2.97 (m, 2H), 2.41 (s, 3H, Ar-CH_3), 1.79-1.72 (m, 2H), 1.51-1.42 (m, 2H), 0.97 (t, J = 7.5 Hz, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=158.2 (s, C=O), 148.2 (s, Ar-C=N), 145.5 (s, Ar-C), 134.5 (s, Ar-C), 134.3 (d, Ar-CH), 131.8 (d, Ar-CH), 129.5 (d, 2 × Ar-CH), 129.3 (d, 2 × Ar-CH), 128.5 (s, Ar-C), 127.8 (d, Ar-CH), 125.0 (d, Ar-CH), 32.2 (t, –CH_2–), 29.8 (t, –CH_2–), 22.5 (t, –CH_2–), 21.7 (q, CH_3), 13.8 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{19}H_{21}N_2O_3S]^+$=$[M+H]^+$: 357.1267; found 357.1271.

2,4-diphenylphthalazin-1(2H)-one (**6fea**): GP-3 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2e** (169.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml), conc. H_2SO_4 (0.39 ml, 4.0 mmol) and *N*-protected hydrazine hydrochloride **8a** (410.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 45 h. Progress of the products **6fea** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6fea** (76.0 mg, 64 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**6fea**)=0.50, UV detection].

2-(4-fluorophenyl)-4-phenylphthalazin-1(2H)-one (**6feb**): GP-3 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2e** (169.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml), conc. H_2SO_4 (0.39 ml, 4.0 mmol) and *N*-protected hydrazine hydrochloride **8b** (455.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 30 h. Progress of the products **6feb** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6feb** (70.0 mg, 55 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**6feb**)=0.50, UV detection].

2-(4-chlorophenyl)-4-phenylphthalazin-1(2H)-one (**6fec**): GP-3 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2e** (169.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml), conc. H_2SO_4 (0.39 ml, 4.0 mmol) and *N*-protected hydrazine hydrochloride **8c** (501.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 43 h. Progress of the products **6feb** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6fec** (80.0 mg, 60 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**6fec**)=0.50, UV detection].

2-(4-bromophenyl)-4-phenylphthalazin-1(2H)-one (**6fed**): GP-3 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2e** (169.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml), conc. H_2SO_4 (0.39 ml, 4.0 mmol) and *N*-protected hydrazine hydrochloride **8d** (625.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 46 h. Progress of the products **6feb** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6fed** (86.0 mg, 57 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**6fed**)=0.40, UV detection].

4-(4-fluorophenyl)-2-tosylphthalazin-1(2H)-one (**6fhe**): GP-3 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2h** (198.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 16 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml), conc. H_2SO_4 (0.39 ml, 4.0 mmol) and *N*-protected hydrazine hydrochloride **8e** (623.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 48 h. Progress of the products **6fhe** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6fhe** (79.0 mg, 50 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**6fhe**)=0.50, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2937, 1719, 1685, 1590, 1451, 1284, 1082, 935, 708 cm^{-1}.^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.42-8.40 (m, 1H, Ar-H), 8.12 (d, J = 8.3 Hz, 2H, Ar-H), 7.79-7.75 (m, 2H, Ar-H), 7.67-7.60 (m, 3H, Ar-H), 7.35 (d, J = 8.3 Hz, 2H, Ar-H), 7.25-7.20 (m, 3H, Ar-H), 2.42 (s, 3H, Ar-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=164.9 (d, Ar-C-F, J = 249 Hz), 157.8 (s, C=O), 147.3 (s, Ar-C=N), 145.8 (s, Ar-C), 134.3 (d, Ar-CH), 134.3 (s, Ar-C), 132.2 (d, Ar-CH), 131.6 (d, Ar-CH), 131.5 (d, Ar-CH), 130.3 (s, Ar-C), 129.6 (d, 2 × Ar-CH), 129.5 (d, 2 × Ar-CH), 129.3 (s, Ar-C), 128.9 (s, Ar-C), 127.8 (d, Ar-CH), 127.2 (d, Ar-CH), 116.0 (d, Ar-CH), 115.8 (d, Ar-CH), 21.7 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{22}H_{19}N_2O_3S]^+$=$[M+H]^+$: 391.1111; found 391.1109.

4-(3,4-dimethoxyphenyl)-2-phenylphthalazin-1(2H)-one (**6fla**)[12b]: GP-3 was followed with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2l** (265.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 20 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml), conc. H_2SO_4 (0.39 ml, 4.0 mmol) and *N*-protected hydrazine hydrochloride **8a** (410.0 mg, 2.8 mmol) and allowed the reaction mixture stirred at 75 °C for 45 h. Progress of the products **6fla** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **6fla** (84.0 mg, 59 %). [TLC control (petroleum ether/ethyl acetate 85:15), R_f(**1f**)=0.90, R_f(**6fla**)=0.30, UV detection].

4-propyl-1H-benzo[d][1,2]oxazin-1-one (**7fa**): GP-4 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2a** (115.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the

reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydroxylamine hydrochloride (138.0 mg, 2.0 mmol) and allowed the reaction mixture stirred at 75 °C for 7 h. Progress of the products **7fa** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **7fa** (46.0 mg, 63 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**7fa**)=0.50, UV detection].

4-butyl-1H-benzo[d][1,2]oxazin-1-one (**7fb**): GP-4 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2b** (137.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 13 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydroxylamine hydrochloride (138.0 mg, 2.0 mmol) and allowed the reaction mixture stirred at 75 °C for 8 h. Progress of the products **7fb** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **7fb** (45.0 mg, 56 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**7fb**)=0.50, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2981, 1690, 1682, 1601, 1543, 1460, 1247, 1089, 914, 713 cm^{-1}.^{1}H NMR ($CDCl_3$, 400 MHz): δ= 8.37 (dd, J = 7.8 Hz and 1.4 Hz, 1H, Ar-H), 7.91 (td, J = 7.7 Hz and 1.2 Hz, 1H, Ar-H), 7.83 (td, J = 7.7 Hz and 1.2 Hz, 1H, Ar-H), 7.71 (d, J = 7.8 Hz, 1H, Ar-H), 2.95-2.91 (m, 2H), 1.79-1.68 (m, 3H), 1.50-1.45 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=163.8 (s, C=O), 155.9 (s, Ar-C=N), 135.3 (d, Ar-CH), 133.4 (d, Ar-CH), 128.8 (d, Ar-CH), 126.9 (s, Ar-C), 124.9 (d, Ar-CH), 122.7 (d, Ar-CH), 30.2 (t, –CH_2–), 29.5 (t, –CH_2–), 22.4 (t, –CH_2–), 13.7 (q, *C*H3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{12}H_{14}NO_2]^+$=$[M+H]^+$: 204.1019; found 204.1023.

4-pentyl-1H-benzo[d][1,2]oxazin-1-one (**7fc**): GP-4 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2c** (160.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 14 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydroxylamine hydrochloride (138.0 mg, 2.0 mmol) and allowed the reaction mixture stirred at 75 °C for 10 h. Progress of the products **7fc** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **7fc** (52.0 mg, 60 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**7fc**)=0.50, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2945, 2876, 1819, 1710, 1680, 1599, 1457, 1280, 1089, 930, 708 cm^{-1}.^{1}H NMR ($CDCl_3$, 400 MHz): δ= 8.38 (dd, J = 7.8 Hz and 0.98 Hz, 1H, Ar-H), 7.91 (td, J = 7.5 Hz and 1.4 Hz, 1H, Ar-H), 7.83 (td, J = 7.5 Hz and 1.4 Hz, 1H, Ar-H), 7.71 (d, J = 8.3 Hz, 1H, Ar-H), 2.94-2.91 (m, 2H), 1.81-1.74 (m, 2H), 1.47-1.31 (m, 4H), 0.90 (t, J = 7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=163.8 (s, C=O), 155.9 (s, Ar-C=N), 135.3 (d, Ar-CH), 133.4 (d, Ar-CH), 128.8 (d, Ar-CH), 126.9 (s, Ar-C), 124.9 (d, Ar-CH), 122.7 (d, Ar-CH), 31.5 (t, –CH_2–), 30.5 (t, –CH_2–), 27.1 (t, –CH_2–), 22.3 (t, –CH_2–), 13.9 (q, *C*H_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{13}H_{16}NO_2]^+$=$[M+H]^+$: 218.1176; found 218.1180.

4-cyclohexyl-1H-benzo[d][1,2]oxazin-1-one (**7fd**): GP-4 was carried out with *ortho*-iodoester **1f** (105.0 mg, 0.40 mmol**)** and aldehyde **2d** (179.0 mg, 1.6 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111.3 mg, 0.48 mmol) and 70% aqueous solution of TBHP (257.1 mg, 2.0 mmol) and allowed the reaction mixture to stir at 120 °C for 12 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoester **1f** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature. Then added ethanol (2 ml) and hydroxylamine hydrochloride (138.0 mg, 2.0 mmol) and allowed the reaction mixture stirred at 75 °C for 12 h. Progress of the products **7fd** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **7fd** (46.0 mg, 50 %). [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.60, R_f(**7fd**)=0.50, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2930, 1719, 1680, 1593, 1450, 1287, 1089, 934, 718 cm^{-1}.^{1}H NMR ($CDCl_3$, 400 MHz): δ= 8.38 (dd, J = 7.8 Hz and 0.98 Hz, 1H, Ar-H), 7.90 (td, J = 7.7 Hz and 1.2 Hz, 1H, Ar-H), 7.81 (td, J = 7.2 Hz and 1.4 Hz, 1H, Ar-H), 7.75 (d, J = 8.3 Hz, 1H, Ar-H), 3.09-3.02 (m, 1H), 2.04-2.01 (m, 2H), 1.93-1.88 (m, 2H), 1.81-1.61 (m, 3H), 1.49-1.28 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=163.7 (s, C=O), 158.7 (s, Ar-C=N), 135.2 (d, Ar-CH), 133.2 (d, Ar-CH), 128.9 (d, Ar-CH), 126.5 (s, Ar-C), 124.4 (d, Ar-CH), 122.8 (d, Ar-CH), 39.6 (d, –CH–), 31.2 (t, 2 ×–CH_2–), 26.4 (t, 2 ×–CH_2–), 25.9 (t, –CH_2–) ppm. HR-MS (ESI^+) m/z calculated for $[C_{14}H_{16}NO_2]^+$=$[M+H]^+$: 230.1176; found 230.1172.

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Keywords One-pot reaction • Acylation • Cyclocondensation • Phthalazines • Phthalazinones • Benzoxazinones • PDE-4 inhibitor

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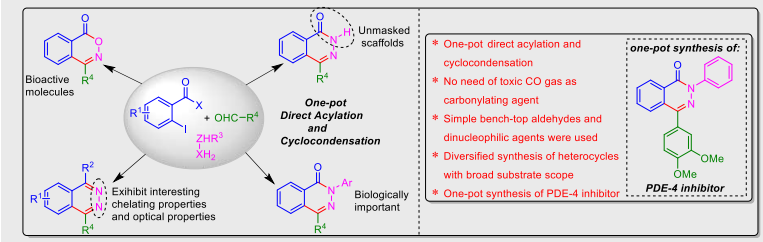

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Palladium-Catalyzed Acylations: A One-pot Diversified Synthesis of Phthalazines, Phthalazinones and Benzooxazinones