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WATER MEDIATED ONE- POT- SYNTHESIS OF 1*H*-PYRAZOLO[1,2-B]PHTHALAZINE-5,10-DIONES AND 2H-INDAZOLO[2,1-B]PHTHALAZINE-1,6,11(13H)-TRIONES

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Abstract
1*H*-pyrazolo[1,2-b]phthalazine-5,10-diones **(5)** and 2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-triones **(7)** have been synthesized by one pot, four-component method. To synthesise them phthalic anhydride **(1)**, hydrazine hydrate **(2)**, benzaldehydes **(3)**and malononitrile **(4a)** /ethyl cynoacetate **(4b)** /dimedone **(6)** in refluxing water for 1-1.5 h in the presence of $InCl_3$ as a catalyst yielding 75-85%. These reactions have an easy workup, provides excellent yields, and uses water as the solvent which is considered to be relatively environmentally benign. The structures of the products were established from their spectral properties IR,^{1}H- NMR, ^{13}C-NMR & Mass spectroscopy.

Introduction:

The development of efficient, economical & environmentally friendly syntheses is an important challenge in modern organic syntheses[I]. In many synthetic organic processes, solvents represent a severe pollution problem. Thus, the replacement of hazardous solvents with relatively green solvents or the altogether elimination of use of hazardous solvents in chemical processes has been one of the key achievements of green chemistry[II]. Based on the principles of green chemistry, a green solvent should meet numerous criteria such as low toxicity, non-volatility, non-mutagenicity, non-flammability and widespread availability among others[III]. In the past decade, water[IV], glycerol[V], polyethylene glycol[VI], ionic liquids[VII] have been used as green solvents in organic reactions. Among all the green solvents, water is the safest, cheapest & non-toxic media-free from economic & environmental problems[VIII]. As a result, serious efforts are being made to develop water as a solvent for most of the organic syntheses and processes wherever possible.

Despite its small presence in natural products phthalazinone nucleus and specifically phthalazin-1(2 system is a versatile scaffold in medicinal chemistry providing developed as enzyme inhibitors, such as aldose reductase (AR) inhibitors[IX], poly(ADP-ribose)polymerase

(PARP) inhibitors[X] or phosphodiesterase (PDE)inhibitors[XI], as ligands acting at G protein-coupled receptors (GPCRs), in particular histamine receptors[XII], adrenoceptors[XIII], dopamine/serotonin receptors[XIV], oradenosine receptors[XV], or even as modulators of ion channel-coupled receptors[XVI] or ligands for nuclear receptors[XVII] derivatives able to interact with different kinds of biological targets.

Phthalazines are also known to have biological activities like antimicrobial[XVIII], anticonvulsant[XIX], antifungal[XX], anticancer[XXI] and anti-inflammatory[XXII].Therefore, a number of methods were reported for syntheses of phthalazine containing derivatives[XXIII]. Recently, syntheses of 1*H*-pyrazolo[1,2-b]phthalazine-5,10-diones was reported by one-pot, three component condensation of phthalhydrazide, malononitrile/ethyl cyanoacetate and benzaldehydes using one of the following conditions:- a) In the presence of p-tolunesulfonic acid as a catalyst and 1-butyl-3-methylimidazolium bromide ([bmim]Br) as ionic liquied at 100 ^{o} C[XXIV], b) In the presence of Triethylamine catalyst in ethanol (5ml) for 60 min under ultrasonication[XXV]. c) In the presence of 1-butyl-3-methylimidazolium hydroxide as ionic liquid under irradiation single-mode microwave 45^{o} C[XXVI.] The syntheses of 1*H*-pyrazolo[1,2-b]phthalazine-5,10-diones were also reported by one pot syntheses of phthalic anhydride, hydrazine, malononitrile / ethyl cynoacetate and derivatives of benzaldehyde using basic ionic liquids like 1,8-diazabicyclo[5.4.0]-undec-7-en-8-ium acetate, pyrrolidinium acetate[XXVII] and triethylamine[XXVIII] as a catalyst with ultrasound-sonication. The latter syntheses (i.e. four component reaction) are very similar to the previous syntheses (i.e. three component reaction) except for the fact that phthalhydrazide has been prepared from phthalic anhydride and hydrazine hydrate in situ in this reaction.

Keeping these results in mind, we now report a study of the four component domino reaction of 1*H*-Pyrazolo[1,2-*b*]phthalazine-5,10-diones **(5)** and 2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-triones **(7)** from phthalic anhydride **(1)** , hydrazine hydrate **(2)**, benzaldehyde **(3)** and malononitrile **(4a)** / ethylcyanoacetate **(4b)** / dimedone **(6)** in the presence of $InCl_3$ as a catalyst in refluxing water.

Results and Discussion:

As illustrated in **scheme -1**, the reaction of phthalic anhydride **(1)** (1mmol/L) with hydrazine hydrate **(2)** (1mmol/L) in refluxing water for 10 min led to the in-situ formation of phthalhydrazide as intermediate. Then, to this reaction mixture was added benzaldehydes **(3a)** (1mmol/L) followed by malononitrile **(4a**) (1mmol/L)and the whole mixture again refluxed in the presence of $InCl_3$ as a catalyst in water for 1 h to form of 1*H*-Pyrazolo[1,2-*b*]phthalazine-5,10-dione **(5a) (Table-1 entry-1)** as the final product. Then, this reaction was examined by carrying out the multi component reaction with **1** (1mmol/L)**, 2**(1mmol/L)**, 3a**(1mmol/L) and **4a**(1mmol/L) in the presence of different solvents (Water, Glycerol, PEG-600, ethylene glycol, DMFand DMSO) at 100 ^{o}C **(Table 1)**. However, multi component reaction of **1, 2, 3a and 4a** in water at 100 ^{o}C for 1 h was found to be the best method giving **5a** in quality and yield greater then 85% (**Table-1, entry1)**. Therefore, water was chosen as the solvent for the further study at 100 ^{o}C.

Scheme-1:

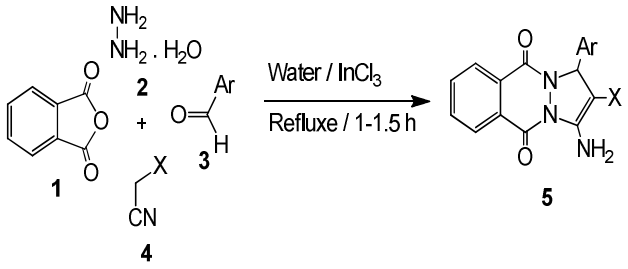


Table-1

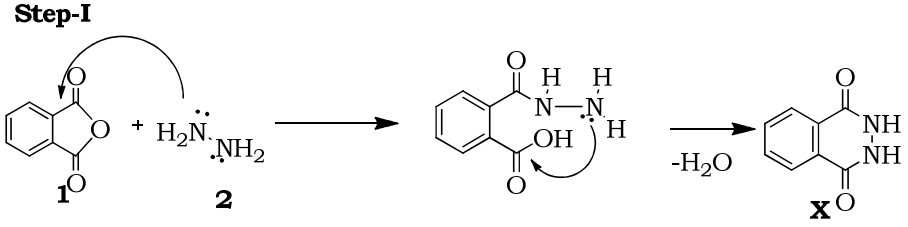
Effect of **Solvent** on reaction of **1**, **2, 3a and 4a** at RT yielding **5a.**

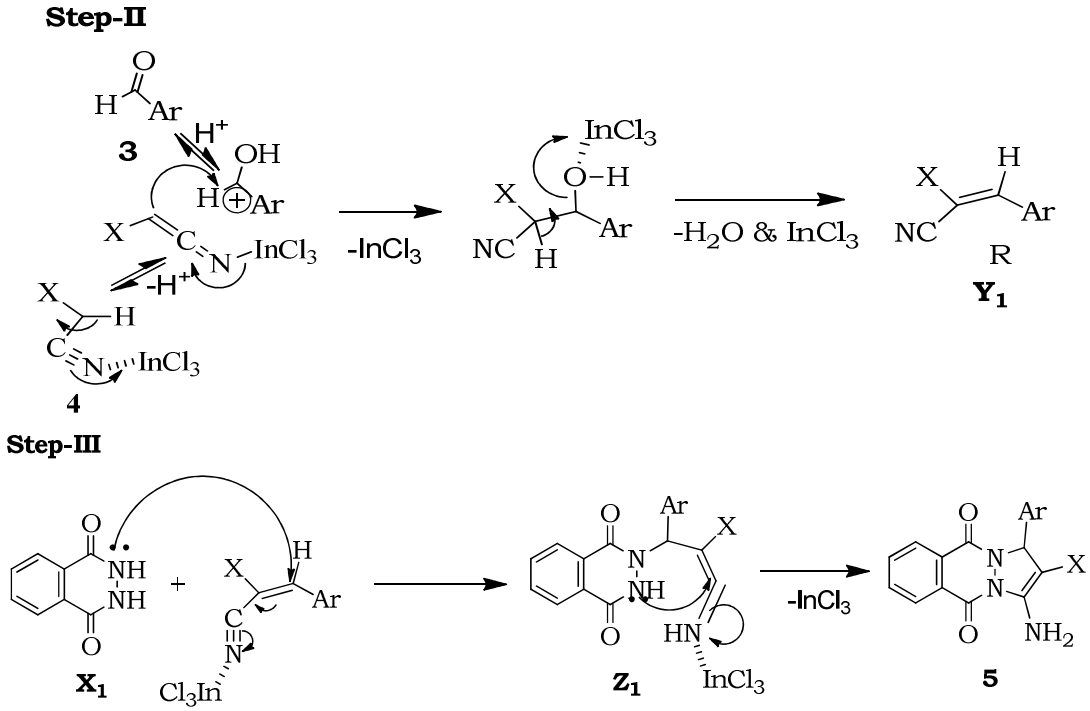
Entry	**Solvent**	**Temperature ^{o}C**	**Time (h)**	**5a (%)**
1	**Water**	**100**	**1**	**85**
2	Glycerol	100	2	70
3	PEG-600	100	2	80
4	Ethylene glycol	100	2	60
5	DMF	100	2	75
6	DMSO	100	2	55

The scope of this one-pot reaction was carried out by varying the structures of benzaldehydes and active methylenes to from **5a-5h** for 1-1.5 h summarized in **Table 2**. Generally, the reactions that employed aromatic aldehydes with electron-withdrawing (-NO_2) or low electron-donating groups (-Cl, -Br) at different positions produced the corresponding products **5**. The structures of the products were established from their spectral properties (^{1}H-NMR, ^{13}C-NMR) and also by comparison with M.P literature data.

A schematic mechanism for the synthesis of titled compounds **5** can be postulated as shown in **Scheme 2**. This mechanism contains three steps. In the first step, formation of phthalhydrazide **(X)** by nucleophilic addition of hydrazine **(2)** to phthalic anhydride (**1)** followed by removal of water molecule. The second step involves forming diene **Y** by standard Knoevenagel condensation of benzaldehydes (**3)** and malononitrile/ethyl cyanoacetate (**4)** followed by removal of water molecule by attacking of $InCl_3$ to –OH group. Then, in the third step, Michael-type addition of the phthalhydrazide **X** to diene **Y** takes place forming the intermediary iminomethylene derivative **z** which undergoes cyclisation affording **5**. **(Scheme-2)**

Scheme-2: Plausible mechanism for **5** from **1, 2, 3** and **4.**





Keeping the above results in our mind, 2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-triones **7a-7f** have been synthesised by one-pot, four component reaction from phthalic anhydride **1**, hydrazine hydrate **2**, benzaldehydes **3a-3f** and dimedone **6** in water at 100 ^{o}C for 1-1.5 h in the presence of $InCl_3$. The yields obtained were good to excellent without formation of any side-products and all reactions proceed rapidly in short times. The structures of the products were established from their spectral properties (^{1}H-NMR, ^{13}C-NMR) and also by comparison with available literature data (supply info) and for literature data see table -2.

Scheme-3:

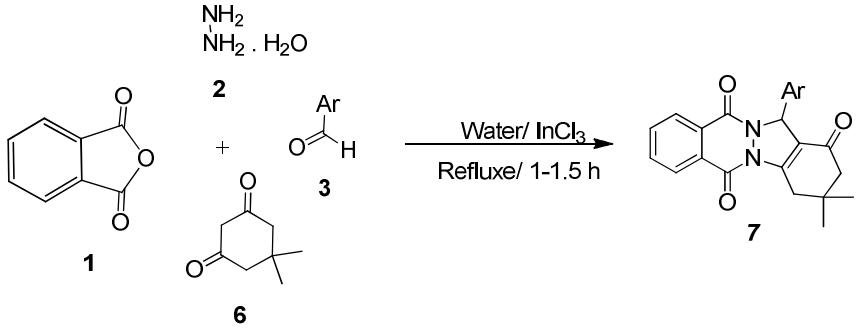


Table-2

Characterization data, reaction time and yields of **5** obtained from **1, 2, 3 and 4** via one-pot, four component syntheses.

Entry	Starting Materials		Product	Yield≠	M.P (Lit M.P)
1	3a (Ar= -Ph)	4a (X= CN)	**5a**	85	275-276 (276-278) [29]
2	3b (Ar = 2-Cl-Ph)	4a (X= CN)	**5b**	82	259-260 (259-261) [30]

3	3c (Ar = 4-Br-Ph)	4a (X= CN)	**5c**	82	263-265 (265-267) [31]
4	3d (Ar = 2-NO_2-Ph)	4a (X= CN)	**5d**	84	229-230 (228-230)[32]
5	3a (Ar= -Ph)	4b (X=COOEt)	**5e**	82	230-231 (232-234)[32]
6	3b (Ar = 2-Cl-Ph)	4b (X=COOEt)	**5f**	82	265-267 (266-267)[31]
7	3c (Ar = 4-Br-Ph)	4b (X=COOEt)	**5g**	84	207-208 (205-206)[31]
8	3d (Ar = 2-NO_2-Ph)	4b (X=COOEt)	**5h**	84	232-233 (230-232)[32]

≠ Refers to yields of crude products only.

Table-3

Characterization data, reaction time and yields of **7** obtained from **1, 2, 3 and 6** via one-pot, four component syntheses.

Entry	Starting Materials		Product	Yield≠	M.P (Lit M.P)
1	3a (Ar= -Ph)	6	**7a**	83	203-205 (204-206)[33]
2	3b (Ar = 2-Cl-Ph)	6	**7b**	82	268-270 (266-269)[33]
3	3c (Ar = 4-Br-Ph)	6	**7c**	81	262-264 (262-263)[33]
4	3d (Ar = 2-NO_2-Ph)	6	**7d**	81	239-240 (238-240)[35]
5	3e (Ar= 3-NO_2-Ph)	6	**7e**	81	267-269 (269-271)[33]
6	3f (Ar = 4-Cl-Ph)	6	**7f**	82	258-259 (258-260)[33]

≠ Refers to yields of crude products only.

Experimental section

Melting points have been uncorrected and determined in open capillary tubes in H_2SO_4 bath.TLC has been run on silica gel-G and visualization has been done using iodine or UV light. IR spectra have been recorded using Perkin-Elmer 1000 instrument in KBr pellets.^{1}HNMR recorded on Bruker Avance have been recorded in DMSO-d^6 using TMS as internal standard at 400 MHz operating frequency.^{13}C NMR recorded by Gemini-varian at 100 MHz operating frequency and Mass spectra have been recorded on Agilent-LCMS instrument.

General procedure for preparation of 5 from 1, 2,3 and 4:

Phthalic anhydride **1** (1.5 g ,10 mmol) and hydrazine hydrate **2** (0.5 ml ,10 mmol) was refluxed in water (5 ml) for 10 min to form phthalhydrazide as intermediate. Then, to this reaction mixture added benzaldehyde **3** (0.96ml ,10 mmol) and malononitrile **4a** (0.6 ml,10 mmol)/ethyl cyanoacetate **4b** (1.0 ml, 10 mmol) in succession, one after another in the presence of $InCl_3$ and the mixture refluxed again for 1-1.5 h. The completion of the reaction was checked with TLC. After that, cold water (50ml) was added to the reaction mixture and neutralized with 10% sodium bicarbonate solution; the solid that separated out was filtered, washed with water (10 ml) and dried. The products was recrystallised with ethanol to obtain **5.**

3-amino-5,10-dioxo-1-phenyl-5,10-dihydro-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (5a): M. P.: 275-276 ^oC; IR (KBr) : 3191-3360 cm^{-1} (-NH-), 2197 (-CN-), 1681 cm^{-1} (-CO-), 1660 cm^{-1} (-CO-); ^{1}H- NMR (DMSO-d_6, 400 MHz): δ 6.12 (s, 1H, -CH), 7.32-8.27 (m, 11H, Ar-H and NH_2); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 61.4, 62.9, 115.9, 126.6, 126.7, 127.2, 128.2, 128.4, 128.6, 128.7, 133.6, 134.6, 138.3, 150.5, 153.6, 156.6; HRMS calcd for $C_{18}H_{12}N_4O_2$ $[M+H]^+$: 317.09652. Found: 317.09380.

3-amino-1-(2-chlorophenyl)-5,10-dioxo-5,10-dihydro-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (5b): M. P.: 259-260 ^{o}C; IR (KBr) : 3181-3370 cm^{-1} (-NH-), 2190 (-CN-),1683 cm^{-1} (-CO-), 1662 cm^{-1} (-CO-);^{1}H- NMR (DMSO-d_6, 400 MHz): δ 6.20 (s, 1H, -CH), 7.22-8.22 (m, 10H, Ar-H and NH_2); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 61.3, 62.8, 115.3, 126.2, 126.5, 127.3, 128.1, 128.5, 128.7, 128.8, 133.3, 134.2, 138.2, 150.4, 153.5, 156.8; HRMS calcd for $C_{18}H_{11}ClN_4O_2$ [M+H]$^{+}$: 351.18653. Found: 351.18967.

3-amino-1-(4-bromophenyl)-5,10-dioxo-5,10-dihydro-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (5c): M. P.: 263-265 ^{o}C; IR (KBr) : 3190-3390 cm^{-1} (-NH-), 2180 (-CN-),1689 cm^{-1} (-CO-), 1669 cm^{-1} (-CO-);^{1}H- NMR (DMSO-d_6, 400 MHz): δ 6.10 (s, 1H, -CH), 7.30-8.28 (m, 10H, Ar-H and NH_2); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 61.0, 62.3, 115.5, 126.1, 126.2, 127.3, 128.2, 128.8, 128.9, 128.9, 133.4, 134.1, 138.3, 150.2, 153.4, 156.6; HRMS calcd for $C_{18}H_{11}BrN_4O_2$ [M+H]$^{+}$: 395.28423. Found: 395.28034.

3-amino-1-(2-nitrophenyl)-5,10-dioxo-5,10-dihydro-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (5d): M. P.: 229-230 ^{o}C; IR (KBr) : 3200-3410 cm^{-1} (-NH-),2210 (-CN-), 1680 cm^{-1} (-CO-), 1668 cm^{-1} (-CO-);^{1}H- NMR (DMSO-d_6, 400 MHz): δ 6.21 (s, 1H, -CH), 7.32-8.24 (m, 10H, Ar-H and NH_2); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 61.1, 62.4, 115.3, 126.0, 126.0, 127.2, 128.0, 128.5, 128.8, 128.9, 133.4, 134.0, 138.2, 150.1, 153.2, 156.5; HRMS calcd for $C_{18}H_{11}N_5O_3$ [M+H]$^{+}$: 362.13310. Found: 362.13612.

Ethyl-3-amino-5,10-dioxo-1-phenyl-5,10-dihydro-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5e): M. P.: 230-231 ^{o}C; IR (KBr) : 3180-3390 cm^{-1} (-NH-), 1732 (-CO-), 1680 cm^{-1} (-CO-), 1670 cm^{-1} (-CO-);^{1}H- NMR (DMSO-d_6, 400 MHz): δ 1.22 (t, 3H, -CH_3), δ 3.88 (t, 2H, -CH_2), δ 6.13 (s, 1H, -CH), 7.22-8.22 (m, 11H, Ar-H and NH_2); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 14.0, 58.9, 61.3, 61.8, 114.8, 124.5, 125.1, 128.0, 128.3, 128.3, 128.7, 128.8, 133.4, 134.3, 138.0, 150.2, 153.2, 156.5, 162.2; HRMS calcd for $C_{20}H_{17}N_3O_4$ [M+H]$^{+}$: 364.13041. Found: 364.13441.

Ethyl-3-amino-1-(2-chlorophenyl)-5,10-dioxo-5,10-dihydro-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5f): M. P.: 265-267 ^{o}C; IR (KBr) : 3162-3370 cm^{-1} (-NH-), 1722 (-CO-), 1685 cm^{-1} (-CO-), 1674 cm^{-1} (-CO-);^{1}H- NMR (DMSO-d_6, 400 MHz): δ 1.12 (t, 3H, -CH_3), δ 3.98 (t, 2H, -CH_2), δ 6.03 (s, 1H, -CH), 7.22-8.23 (m, 10H, Ar-H and NH_2); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 14.2, 58.5, 61.5, 61.9, 114.3, 124.0, 124.2, 125.1, 126.2, 127.2, 127.4, 128.3, 132.3, 133.4, 137.1, 151.3, 153.3, 155.1, 160.2; HRMS calcd for $C_{20}H_{16}ClN_3O_4$ [M+H]$^{+}$: 398.24039. Found: 398.24339.

Ethyl-3-amino-1-(4-bromophenyl)-5,10-dioxo-5,10-dihydro-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5g): M. P.: 207-209 ^{o}C; IR (KBr) : 3012-3360 cm^{-1} (-NH-), 1713 (-CO-), 1675 cm^{-1} (-CO-), 1670 cm^{-1} (-CO-);^{1}H- NMR (DMSO-d_6, 400 MHz): δ 1.30 (t, 3H, -CH_3), δ 3.76 (t, 2H, -CH_2), δ 6.04 (s, 1H, -CH), 7.21-8.23 (m, 10H, Ar-H and NH_2); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 14.4, 56.6, 61.4, 61.7, 113.2, 120.3, 124.3, 124.9, 126.1, 126.7, 126.9, 128.2, 132.0, 133.3, 136.0, 150.2, 153.2, 154.0, 161.3; HRMS calcd for $C_{20}H_{16}BrN_3O_4$ [M+H]$^{+}$: 442.13242. Found: 442. 13642.

Ethyl-3-amino-1-(2-nitrophenyl)-5,10-dioxo-5,10-dihydro-1H-pyrazolo[1,2-b]phthalazine-2-carboxylate (5h): M. P.: 232-233 ^{o}C; IR (KBr) : 3100-3364 cm^{-1} (-NH-), 1712 (-CO-), 1679 cm^{-1} (-CO-), 1672 cm^{-1} (-CO-);^{1}H- NMR (DMSO-d_6, 400 MHz): δ 1.20 (t, 3H, -CH_3), δ 3.86 (t, 2H, -CH_2), δ 6.02 (s, 1H, -CH), 7.21-8.23 (m, 10H, Ar-H and NH_2); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 14.2, 56.4, 61.2, 61.5, 113.1, 120.2, 124.4, 124.8, 126.4, 126.6, 126.8, 128.1, 132.1, 133.3, 136.0, 150.2, 153.1, 154.0, 161.0; HRMS calcd for $C_{20}H_{16}N_4O_5$ [M+H]$^{+}$: 409.12567. Found: 409.12867.

General procedure for preparation of 7 from 1, 2,3 and 6:

Phthalic anhydride **1** (1.5 g ,10 mmol) and hydrazine hydrate **2** (0.5 ml ,10 mmol) was refluxed in water (5 ml) for 10 min to form phthalhydrazide as intermediate. Then, to this

reaction mixture added benzaldehyde **3** (0.96ml ,10 mmol) and dimedone **6**(1.4 g ,10 mmol) in succession, one after another in the presence of $InCl_3$ and the mixture refluxed again for 1-1.5 h. The completion of the reaction was checked with TLC. After that, cold water (50ml) was added to the reaction mixture and neutralized with 10% sodium bicarbonate solution; the solid that separated out was filtered, washed with water (10 ml) and dried. The products was recrystallised with ethanol to obtain **7.**

3,3-dimethyl-13-phenyl-3,4-dihydro-1H-indazolo[1,2-b]phthalazine-1,6,11(2H,13H)-trione (7a): M. P.: 203-205 ^oC; IR (KBr) : 1661 (-CO-), 1625 cm^{-1} (-CO-), 1601 cm^{-1} (-CO-); ^1H- NMR (DMSO-d_6, 400 MHz): δ 0.89-1.03 (s, 6H, -$2CH_3$), δ 2.05-2.54 (s, 4H, -$2CH_2$), δ 4.54 (s, 1H, -CH), 7.09-8.08 (m, 9H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 26.3, 28.7, 31.2, 31.8, 50.0, 114.4, 125.1, 126.1, 127.8, 128.0, 132.5, 144.2, 154.6, 162.8, 196.0; HRMS calcd for $C_{23}H_{20}N_2O_3$ $[M+H]^+$: 373.1268. Found: 373. 1238.

13-(2-chlorophenyl)-3,3-dimethyl-3,4-dihydro-1H-indazolo[1,2-b]phthalazine-1,6,11(2H,13H)-trione (7b): M. P.: 268-270 ^oC; IR (KBr) : 1670 (-CO-), 1655 cm^{-1} (-CO-), 1631 cm^{-1} (-CO-); ^1H- NMR (DMSO-d_6, 400 MHz): δ 0.99-1.04 (s, 6H, -$2CH_3$), δ 2.15-2.54 (s, 4H, -$2CH_2$), δ 4.53 (s, 1H, -CH), 7.19-8.08 (m, 8H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 24.4, 28.6, 30.1, 32.5, 50.3, 114.3, 124.2, 126.5, 127.4, 128.1, 131.4, 143.1, 153.3, 162.5, 196.1; HRMS calcd for $C_{23}H_{19}ClN_2O_3$ $[M+H]^+$: 408.1453. Found: 408.1483.

13-(4-bromophenyl)-3,3-dimethyl-3,4-dihydro-1H-indazolo[1,2-b]phthalazine-1,6,11(2H,13H)-trione (7c): M. P.: 262-264 ^oC; IR (KBr) : 1672 (-CO-), 1642 cm^{-1} (-CO-), 1622 cm^{-1} (-CO-); ^1H- NMR (DMSO-d_6, 400 MHz): δ 0.91-1.34 (s, 6H, -$2CH_3$), δ 2.12-2.53 (s, 4H, -$2CH_2$), δ 4.50 (s, 1H, -CH), 7.14-8.14 (m, 8H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 24.2, 28.1, 30.2, 32.2, 50.2, 114.2, 123.2, 126.2, 127.3, 128.2, 131.0, 143.2, 153.2, 162.4, 196.1; HRMS calcd for $C_{23}H_{19}BrN_2O_3$ $[M+H]^+$: 451.2372. Found: 451.2343.

13-(2-nitrophenyl)-3,3-dimethyl-3,4-dihydro-1H-indazolo[1,2-b]phthalazine-1,6,11(2H,13H)-trione (7d): M. P.: 239-240 ^oC; IR (KBr) : 1674 (sharp, strong, -CO-group), 1652 cm^{-1} (-CO-), 1632 cm^{-1} (sharp, strong, -CO-of amide group); ^1H- NMR (DMSO-d_6, 400 MHz): δ 0.92-1.24 (s, 6H, -$2CH_3$), δ 2.13-2.52 (s, 4H, -$2CH_2$), δ 4.52 (s, 1H, -CH), 7.16-8.04 (m, 8H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 24.3, 28.2, 30.2, 32.3, 50.2, 114.1, 123.2, 126.3, 127.3, 128.3, 131.1, 143.2, 153.2, 162.5, 196.2; HRMS calcd for $C_{23}H_{19}N_3O_4$ $[M+H]^+$: 418.1330. Found: 418.1360.

13-(3-nirophenyl)-3,3-dimethyl-3,4-dihydro-1H-indazolo[1,2-b]phthalazine-1,6,11(2H,13H)-trione (7e): M. P.: 267-269 ^oC; IR (KBr) : 1672 (-CO-), 1662 cm^{-1} (-CO-), 1651 cm^{-1} (-CO-); ^1H- NMR (DMSO-d_6, 400 MHz): δ 0.92-1.23 (s, 6H, -$2CH_3$), δ 2.13-2.54 (s, 4H, -$2CH_2$), δ 4.49 (s, 1H, -CH), 7.18-8.04 (m, 8H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 24.2, 28.0, 30.1, 32.3, 50.1, 114.1, 123.3, 126.4, 127.3, 128.2, 131.0, 143.1, 153.1, 162.4, 195.9; HRMS calcd for $C_{23}H_{19}N_3O_4$ $[M+H]^+$: 418.1330. Found: 418.1372.

13-(4-chlorophenyl)-3,3-dimethyl-3,4-dihydro-1H-indazolo[1,2-b]phthalazine-1,6,11(2H,13H)-trione (7f): M. P.: 258-259 ^oC; IR (KBr) : 1670 (-CO-), 1660 cm^{-1} (-CO-), 1653 cm^{-1} (-CO-); ^1H- NMR (DMSO-d_6, 400 MHz): δ 0.99-1.24 (s, 6H, -$2CH_3$), δ 2.03-2.53 (s, 4H, -$2CH_2$), δ 4.44 (s, 1H, -CH), 7.14-8.03 (m, 8H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 24.3, 28.5, 30.1, 32.3, 50.2, 114.3, 123.3, 126.2, 127.3, 128.2, 131.0, 143.3, 153.1, 162.4, 195.8; HRMS calcd for $C_{23}H_{19}ClN_2O_3$ $[M+H]^+$: 408.1453. Found: 408.1492.

Conclusion:

In summary, a novel method to prepare 1*H*-pyrazolo[1,2-b]phthalazine-5,10-diones and 2Hindazolo[2,1-b]phthalazine-1,6,11(13H)-triones have been developed in one-pot by condensation of phthalic anhydride hydrazine hydrate, benzaldehyde, malononitrile/ethylcyanoacetate and dimedone under Green Condition. Significant rate

acceleration of the reaction in water observed and compared to commonly use of green solvents. Through this reaction, variety of **5/7** synthesized in water with good yield**.**

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