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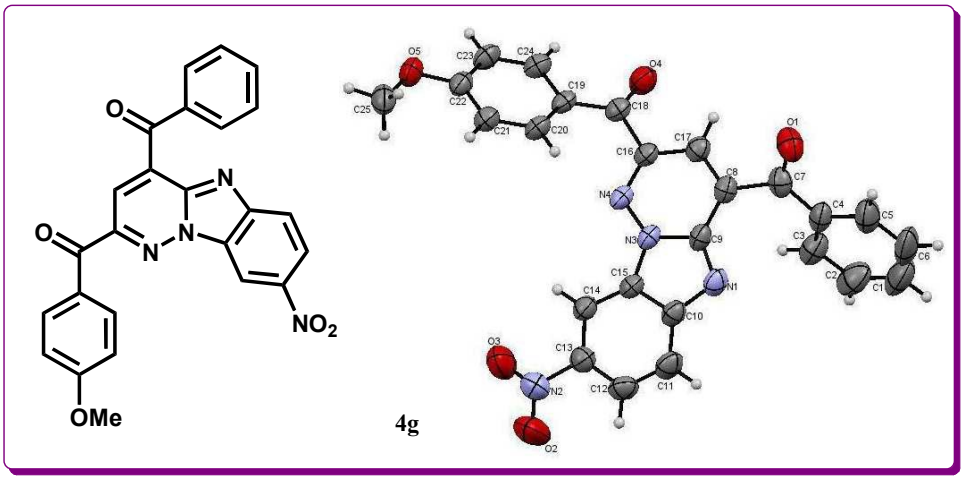

Microwave-Assisted Synthesis in Water: First one-pot Synthesis of A novel Class of Polysubstituted Benzo[4,5]imidazo[1,2-*b*]pyridazines *via* Intramolecular S_NAr

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Abstract

A novel and straightforward one-pot synthesis protocol has been developed for the synthesize of benzo[4,5]imidazo[1,2-*b*]pyridazines through intramolecular S_NAr, utilizing water as green solvent and microwave as efficient green energy source. The entire strategy consist of just one step, reaction between 3-oxo-2-arylhydrazonopropanals which contain *o*-fluorine substituent on the *N*-aryl ring of the arylhydrazone moieties with active methylene compounds, including 3-oxo-3-phenylpropionitrile, 3-oxo-3-hetarylpropionitrile, ethyl cyanoacetate and 2-cyano-acetamide giving the target compounds in an overall yield of 89-99 %. The reaction is carried out under microwave irradiation as well as under conventional heating. The factors affecting the optimization of the reaction are examined in details. X-ray crystallographic analysis was used in the establishment of structures and regioselectivity of the reaction.

Keywords

benzo[4,5]imidazo[1,2-*b*]pyridazine; 3-oxo-2-arylhydrazonopropanal; microwave irradiation; intramolecular SNAr

Introduction

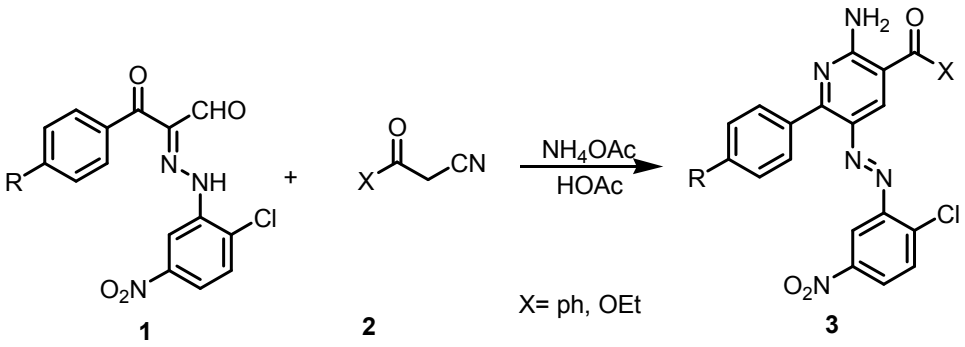
A large number of condensed heterocyclo-benzimidazoles are well known since the benzimidazole ring displays an important heterocyclic pharmacophore in drug discovery.[1,2] A wide variety of synthetic methods for their preparation are available not only because of academic interests but also due to their multifarious biological activities including, antibacterial,[3-5] antihelminthic,[6] antiviral,[7,8] anticancer,[9-11] antiprotozoal,[12,13] antifungal, anti-inflammatory and analgesic activities.[10,14] On the other hand, the considerable biological and medicinal activities of the pyridazines and their derivatives have also attracted continuing interest over the years because of their varied biological activities exemplified as antituberculosis,[15-17] antimicrobial,[18-20] antibacterial and antifungal,[21] antihypertensive,[22] anticancer,[23] herbicidal,[24] anti-inflammatory activities,[25] and protein tyrosine phosphatase 1B (PTP1B) inhibitors.[26] Moreover the pyridazines have been found to be highly active insecticides.[27] Also they act as plant growth regulators and crop protection agents in the field of agricultural science.[28] So, on the basis of the above findings the benzimidazole and pyridazine are privileged structures, which attracted considerable attention in the designing of biologically active molecules and combining them in one molecule exemplified by the benzo[4,5]imidazo-pyridazine system it is expected to furnish biologically active molecule with characteristic features. Recently, green or sustainable chemistry has attained the status of a major scientific discipline and the studies in this area have led to the development of cleaner and relatively benign chemical processes with many new technologies being developed each year.[29] Among them, much effort has been devoted to the use of nontraditional and eco-friendly solvents for chemical synthesis. One of these unconventional media is the water especially in conjunction with microwave irradiation for conducting the organic reactions. The use of water as solvent

features many benefits such as improving reactivities and selectivities, simplifying the workup procedures, enabling recycling of the catalysts, allowing mild reaction conditions and high efficiency in many organic reactions. In addition, the water nontoxic and readily available at low cost, it is also nonflammable and environmentally benign, providing opportunities for clean processing and pollution prevention.[30] However, after detailed literature survey it was observed that there were only publications devoted to the synthesis of imidazo[1,2-*b*]pyridazine,[31,32] and not benzo[4,5]imidazo[1,2-*b*]pyridazine to the best of our knowledge. So in continuation of our research program on the synthesis of condensed azines and nitrogen heterocycles,[33-35] we report here the first example of microwave assisted one-pot synthesis protocol for benzo[4,5]-imidazo[1,2-*b*]pyridazines utilizing water through intramolecular exocyclic cyclization which involve nucleophilic aromatic substitution of fluorine. The X-ray single crystal technique as an advanced tool of analysis was employed in this study for structure elucidation and for determination the regioselectivety of the reactions.

Results and Discussion

In earlier investigations, we have developed new and general strategies for the synthesis of 2-amino-5-arylazonicotinates and pyridazinones that involve reactions of 3-oxo-2-arylhydrazonopropanals **1** with active methylene compounds. As part of these studies, we also investigated the utility of 2-amino-5-arylazonicotinates in routes for the synthesis of condensed pyrazolopyridines and polycyclic fused pyridines.[33-36] In continuing efforts aimed at the design of novel routes for the preparation of important *N*-heterocyclic compounds, we planned to employ reactions of 3-oxo-2-arylhydrazonopropanals **1** with active methylene compounds to prepare the targeted benzimidazolopyridazine fused system. Previously it was demonstrated that the reactions of 3-oxo-2-arylhydrazonopropanals containing electron poor arylhydrazone groups,

which possess two electron withdrawing nitro and Cl groups on the aryl ring of this moiety, react with 3-oxo-3-phenylpropionitrile (**2a**) or ethyl cyanoacetate (**2b**) to form the corresponding 2-amino-6-aryl-5-arylazopyridines **3** as the sole isolable products (**Scheme 1**).[35,36]



Scheme 1. Preparation of 2-amino-6-aryl-5-arylazo-3-benzoylpyridines **3.**

In contrast to this finding it was observed that reactions of 3-oxo-2-aryl-hydrazonopropanals which contain *o*-fluorine substituent and NO_2 group on the *N*-aryl ring of the arylhydrazone moieties with active methylene compounds pursing a different path to give the benzo[4,5]imidazo[1,2-*b*]pyridazine ring system. Herein, we have been developing the protocol for the direct one-pot synthesis of benzo[4,5]imidazo[1,2-*b*]pyridazine derivatives which involving the intramolecular exocyclic cyclization using water and microwave irradiation. The reaction conditions were optimized using 2-[2-(2-fluoro-5-nitrophenyl)hydrazono]-3-oxo-3-phenylpropanal (**1a)**, with 3-oxo-3-phenylpropionitrile (**2a**) as the model substrates, and the effect of parameters like choice of solvent, type of the used additives, mode of activation (microwave irradiation and conventional heating) will be examined and the results are summarized in Table 1. Firstly, we will apply the same reaction condition that used in our previous work AcOH/$AcONH_4$ as reaction medium, which afford only one isolable product. The HRMS of the obtained pure product showed a peak at *m/z* 422.1012, this value corresponds to

the molecular formula $C_{24}H_{14}N_4O_4$. Also the ^{1}H NMR spectrum of the reaction product revealed sets of 14 aromatic protons signals in the region δ 7.61- 8.71, in addition to a singlet signal at δ 8.35 due to the pyridazine H-3, which is typically close to analogously reported pyridazine H proton at δ ≈ 8.3 ppm,[34] and deviod any signals due to the imine NH or NH_2 protons. These data support the benzo[4,5]imidazo[1,2-*b*]pyridazine structure **4a** and rules out the pyridazinimine open structure **5** or the 2-amino-5-arylazopyridine structure **6** (**Scheme 2**). Moreover the benzo[4,5]imidazo[1,2-*b*]pyridazine structure was unequivocally evidenced by measuring the X-ray single crystal analysis for **4g** (**Figure 1**). Secondly, the effect of additive was investigated (entries 1−3), it was found that the anhydrous AcONa afford 4**a** in excellent yields, whereas other additives, such as $AcONH_4$ and K_2CO_3 were less effective. Then, we probed the influence of different solvents on the reaction (entries 4−8). Water and acetic acid were found to be effective solvents for good results. DMF, dioxane and EtOH were found to be less effective. The yield of the product **4a** under microwave irradiation using H_2O/AcONa, at 120 °C (250 watt, 10 min), or AcOH/AcONa at 125 °C (250 watt, 15 min) was found to be 99% and 98% respectively, however, when the same reaction was repeated under conventional heating at reflux the reaction completed after 3 hours in case of water and after 6 hours in case of acetic acid, but with noticeable lack in the isolated yield 74 % (entrie 7) and 69% (entrie 2). But the use of water as solvent possess some features such as environmentally benign, providing opportunities for clean processing and pollution prevention. Finally the neat condition was applied for this reaction either using microwave irradiation or conventional heating, but the isolated yield in both cases proved that this condition less effective.

Table 1. Optimization of the reaction conditions for the synthesis of 4a [a].

Entry	Solvent	Additive	Yield% of 4a[a] MW[b]	Yield% of 4a[a] Δ[c]
1	Acetic acid	$AcONH_4$	77	53
2	**Acetic acid**	**AcONa**	**98**	**69**
3	Acetic acid	K_2CO_3	64	45
4	DMF	AcONa	81	64
5	Dioxane	AcONa	76	58
6	EtOH	AcONa	Trace[d]	None
7	**H_2O**	**AcONa**	**99**	**74**
8	None	AcONa	53[e]	41[f]

[a] Reaction conditions: 2-[2-(2-fluoro-5-nitrophenyl)hydrazono]-3-oxo-3-phenylpropanal (**1a**) (2 mmoles) and with 3-oxo-3-phenylpropionitrile (**2a**) (2 mmoles), additive (3 mmoles) in solvent (7 mL) under microwave irradiation (250 watt) (at 125 °C for 15 min in case of AcOH, at 120 °C for 10 min in case of water) or conventional heating (at reflux for 6 h in case of AcOH, for 3h in case of water).
MW[b] = Microwave irradiation, **Δ**[c] = conventional heating.
[d] The starting materials **1a** and **2a** were almost recovered.
[e] Fusion in MW at 160 °C for 10 min (250 watt).
[e] Fusion in an oil bath at 175 °C for 15 min.

Moreover the role of MW power output, in addition to the effect of time and temperature on the course of the reaction was studied as show in table **3**. The microwave power of 250 watt was found to be the best power level for conducting the desired reaction at 125 °C for 15 min in case of acetic acid and at 120 °C for 10 min in case of water.

Table 2. Optimization of the microwave power, temperature and time for the synthesis of **4a**[a].

Entry	Temperature (°C)	Power (watt)	Time (min)	Yield% of 4a
1	100	150	15	None[b]
2	100	150	30	Trace[c]
3	125	150	15	14
4	125	200	15	56
5	125	250	15	98

[a] Reaction conditions: 2-[2-(2-fluoro-5-nitrophenyl)hydrazono]-3-oxo-3-phenylpropanal (**1a**) (2 mmoles) and with 3-oxo-3-phenylpropionitrile (**2a**) (2 mmoles), additive (3 mmoles) in acetic acid (7 mL)
[b]The starting materials **1a** and **2a** were completely recovered.
[c]The starting materials **1a** and **2a** were almost recovered.

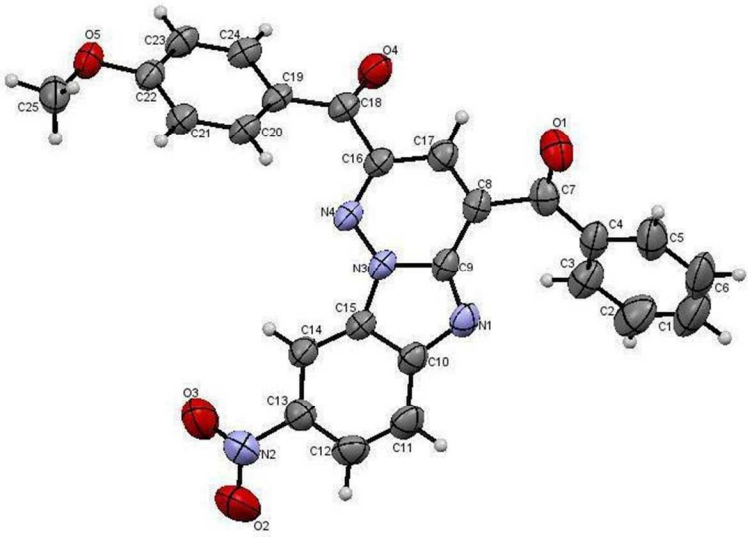
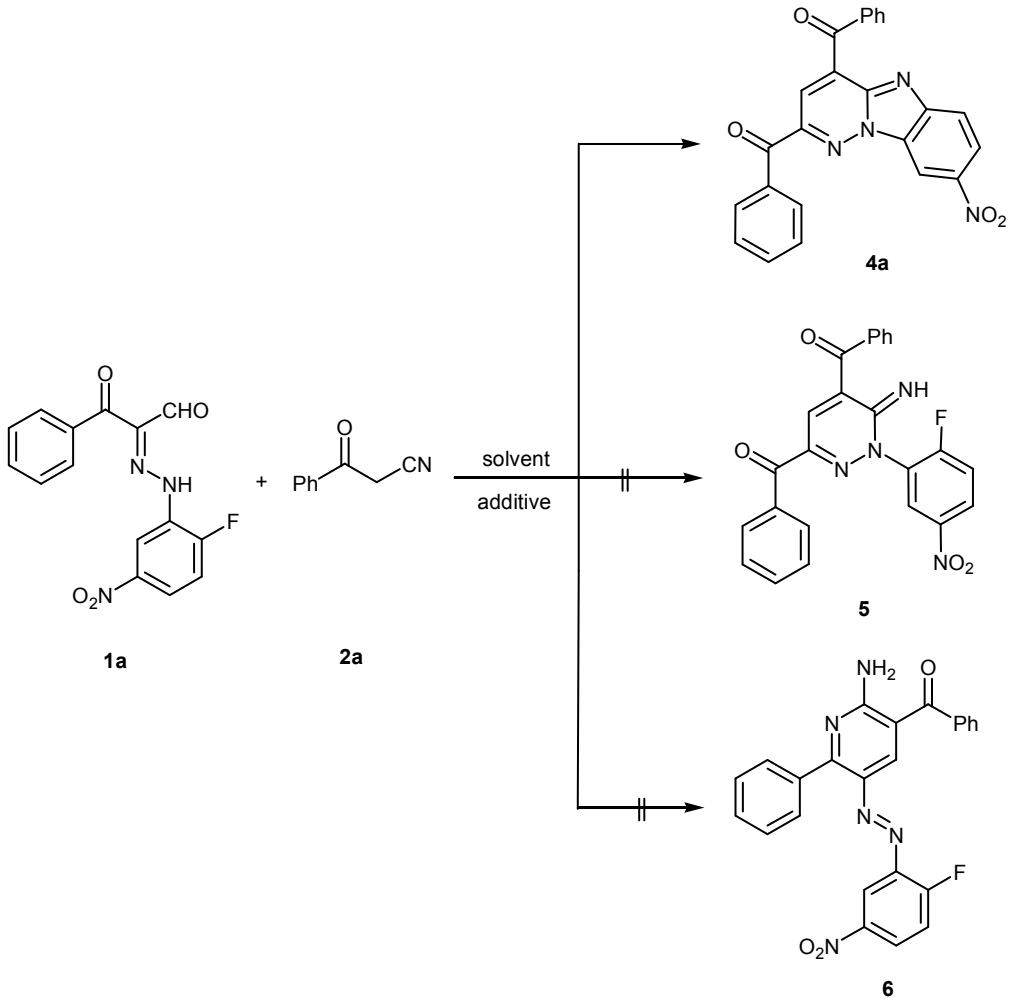
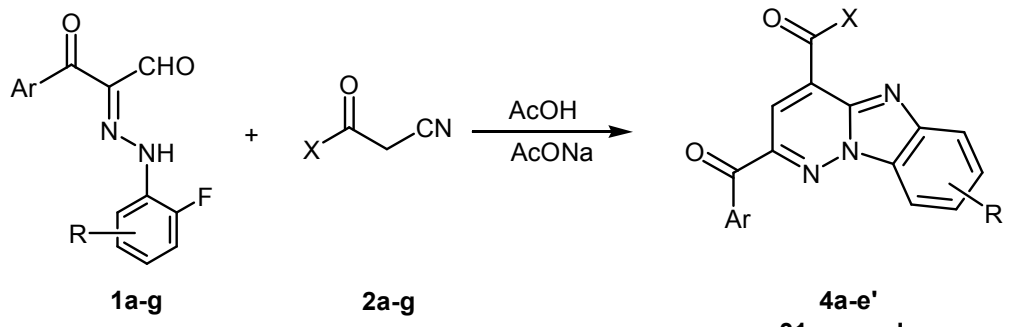


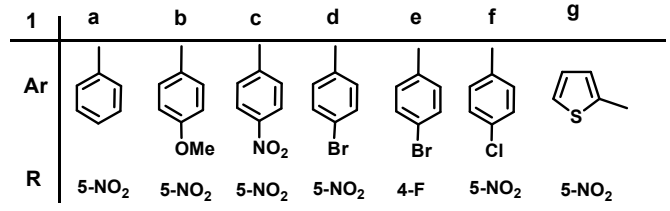
Figure 1. ORTEP plot of the X-ray crystallographic data determined for **4g**.

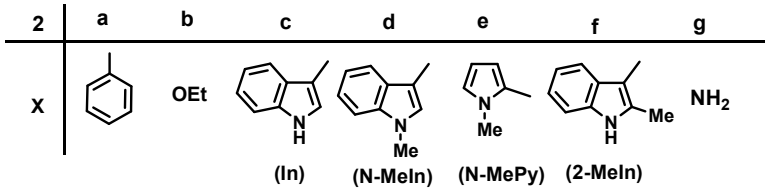


Scheme 2. Synthesis of (4-benzoyl-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-2-yl)phenylmethanone (**4a**).

With the optimized reaction conditions in hand, the scope and generality of this method for synthesizing benzo[4,5]imidazo[1,2-*b*]pyridazine derivatives **4** was investigated. The methodology was found to be applicable to a wide range of the substrates; 3-oxo-2-arylhydrazonopropanal derivatives which contain *o*-fluorine substituent on the *N*-aryl ring of the arylhydrazone moieties **1a-g** and active methylene compounds **2a-g**. Thus, the reaction of the arylhydrazonopropanals **1a-g** with the active methylene compounds **2a-g** was conducted using either H_2O/AcONa or AcOH/AcONa system under both microwave irradiation and conventional heating to afford the corresponding benzo[4,5]imidazo[1,2-*b*]pyridazine derivatives **4 a-e'**, (**Scheme 3**).







Scheme3 **.** Synthesis of the benzimidazolo[1,2-*b*]pyridazine derivatives (**4a-e**`).

Table 3. The reactions of 3-oxo-2-arylhydrazonopropanals **1a-g** with 3-oxopropionitrile derivatives **2a-g.**

Entry	Reactants	Products	Ar	R	X	Yield% of 4[a] MW (H_2O/AcOH)	Yield% of 4[a] Δ (H_2O/AcOH)
1	1a + 2a	**4a**	C_6H_5	5-NO_2	C_6H_5	99/98	74/69
2	1a + 2b	**4b**	C_6H_5	5-NO_2	OEt	99/99	85/67
3	1a + 2c	**4c**	C_6H_5	5-NO_2	In	97/94	72/66
4	1a + 2d	**4d**	C_6H_5	5-NO_2	N-MeIn	96/93	77/68
5	1a + 2e	**4e**	C_6H_5	5-NO_2	N-MePy	98/96	75/71
6	1a + 2g	**4f**	C_6H_5	5-NO_2	NH_2	97/97	69/54
7	1b + 2a	**4g**	4-$MeOC_6H_4$	5-NO_2	C_6H_5	95/93	71/65
8	1b + 2b	**4h**	4-$MeOC_6H_4$	5-NO_2	OEt	99/96	80/69
9	1b + 2c	**4i**	4-$MeOC_6H_4$	5-NO_2	In	96/95	68/63
10	1b + 2d	**4j**	4-$MeOC_6H_4$	5-NO_2	N-MeIn	94/91	66/54
11	1b + 2e	**4k**	4-$MeOC_6H_4$	5-NO_2	N-MePy	98/97	74/70
12	1b + 2f	**4l**	4-$MeOC_6H_4$	5-NO_2	2-MeIn	93/89	64/51
13	1b + 2g	**4m**	4-$MeOC_6H_4$	5-NO_2	NH_2	94/95	67/55
14	1c + 2a	**4n**	4-$NO_2C_6H_4$	5-NO_2	C_6H_5	99/99	81/73
15	1c + 2b	**4o**	4-$NO_2C_6H_4$	5-NO_2	OEt	99/94	83/66
16	1c + 2c	**4p**	4-$NO_2C_6H_4$	5-NO_2	In	98/98	77/74
17	1c + 2d	**4q**	4-$NO_2C_6H_4$	5-NO_2	N-MeIn	98/97	72/71
18	1c + 2e	**4r**	4-$NO_2C_6H_4$	5-NO_2	N-MePy	96/98	75/70
19	1c + 2f	**4s**	4-$NO_2C_6H_4$	5-NO_2	2-MeIn	89/90	60/55
20	1c + 2g	**4t**	4-$NO_2C_6H_4$	5-NO_2	NH_2	94/95	73/66
21	1d + 2a	**4u**	4-BrC_6H_4	5-NO_2	C_6H_5	91/89	59/53
22	1d + 2b	**4v**	4-BrC_6H_4	5-NO_2	OEt	95/90	63/60
23	1d + 2c	**4w**	4-BrC_6H_4	5-NO_2	In	93/92	66/58
24	1d + 2d	**4x**	4-BrC_6H_4	5-NO_2	N-MeIn	90/91	63/59
25	1e + 2c	**4y**	4-BrC_6H_4	4-F	In	93/95	78/71
26	1e + 2d	**4z**	4-BrC_6H_4	4-F	N-MeIn	94/92	76/73
27	1f + 2c	**4a`**	4-ClC_6H_4	5-NO_2	In	96/93	72/61
28	1g + 2c	**4b`**	C_4H_3S	5-NO_2	In	95/95	64/63
29	1g + 2d	**4c`**	C_4H_3S	5-NO_2	N-MeIn	99/97	71/68
30	1g + 2e	**4d`**	C_4H_3S	5-NO_2	N-MePy	93/94	63/65
31	1g + 2g	**4e`**	C_4H_3S	5-NO_2	NH_2	95/98	68/67

[a]*Reaction conditions*: 3-oxo-2-arylhydrazonopropanals **1a-g** (2 mmoles) with 3-oxopropionitrile derivatives **2a-g** (2 mmoles), AcONa (3 mmoles) in AcOH/ (7mL) under microwave irradiation (250 watt) (at 125 °C for 15 min) or conventional heating (at reflux for 6 h); or 3-oxo-2-arylhydrazonopropanals **1a-g** (2 mmoles) with 3-oxopropionitrile derivatives **2a-g** (2 mmoles), AcONa (3 mmoles) in H_2O (7mL) under microwave irradiation (250 watt) (at 120 °C for 10 min) or conventional heating (at reflux for 3h).

The yields of the products **4a-e'** varied between 89 - 99% after 10 or 15 min of microwave irradiation in case of water and acetic acid respectively, and between 51 - 85 % after 3 or 6 h of conventional heating as shown in Table **3**. So it is clear that the yields of **4a** in both cases using either water or acetic acid is very tight in most instances by using microwave

irradiation, but the use of water as green solvent was advantaged than acetic acid. Similar to compound **4a**, the structures of **4b-e**` were determined from their full spectral data (IR, HRMS, ^{1}H and ^{13}C NMR spectra) and in representative cases by X-ray crystallographic analysis for compounds **4u**, **4w** and **4y** as depicted in Figures **2-4**.

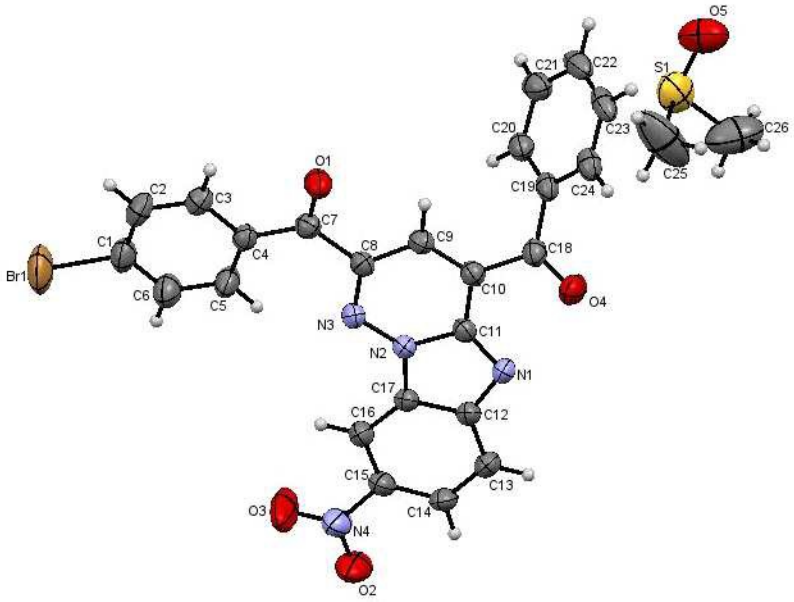


Figure 2. ORTEP plot of the X-ray crystallographic data determined for **4u**.

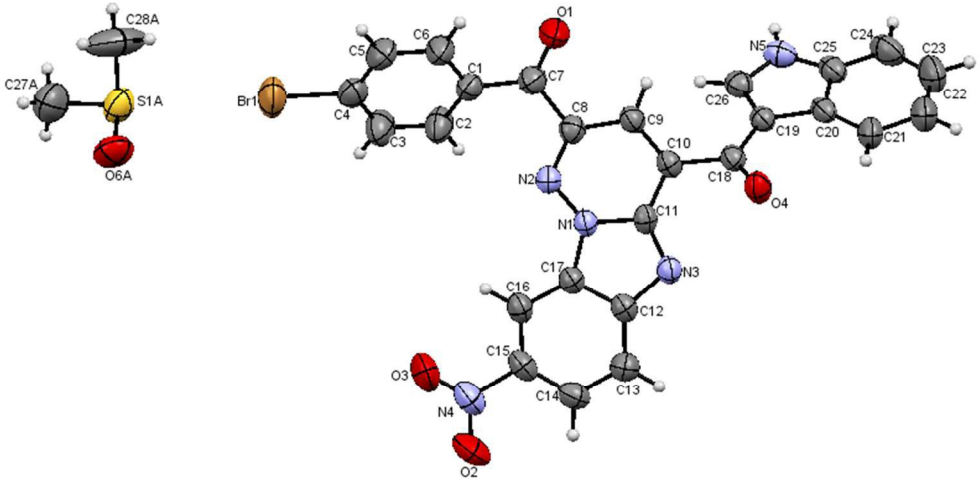


Figure 3. ORTEP plot of the X-ray crystallographic data determined for **4w**.

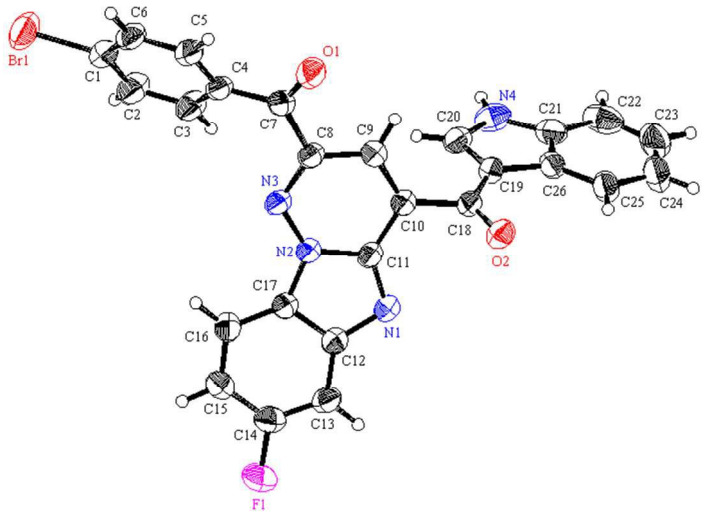
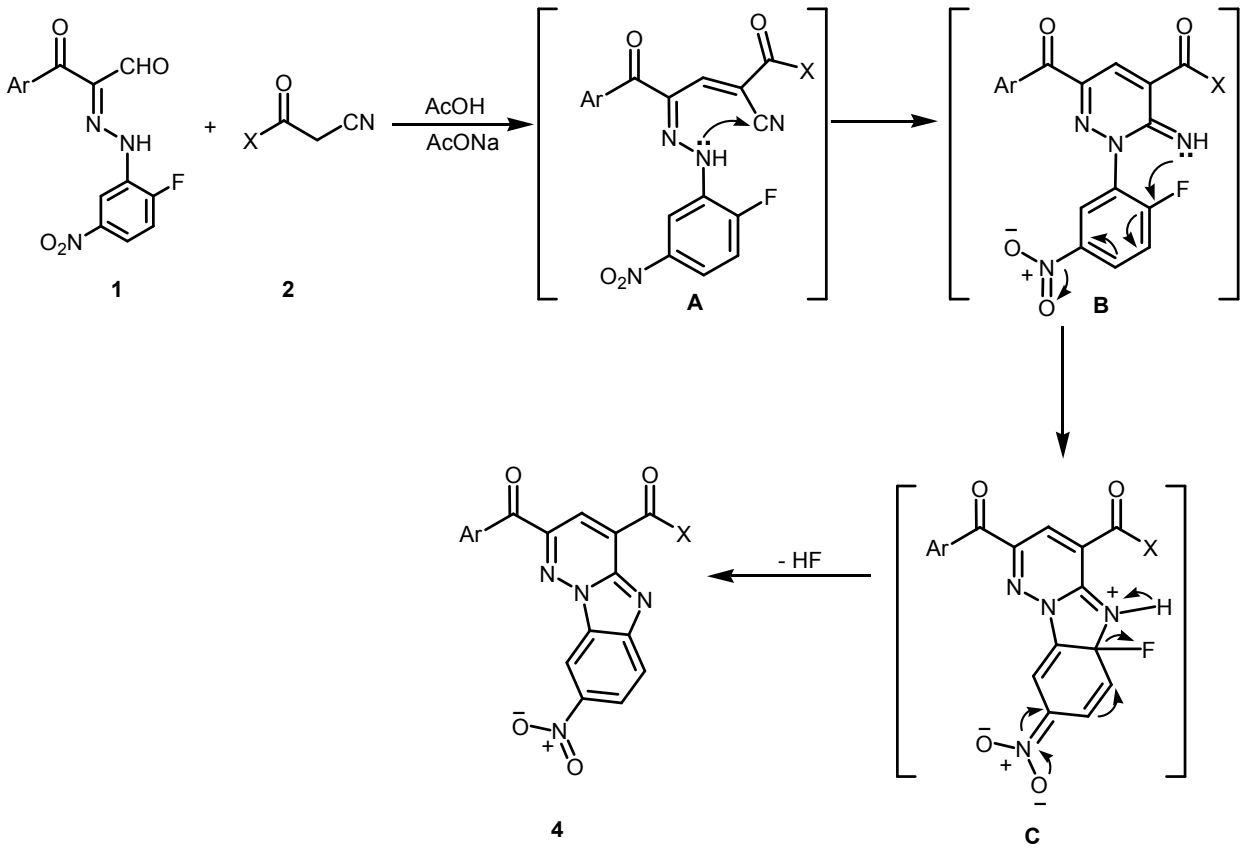


Figure 4. ORTEP plot of the X-ray crystallographic data determined for **4y**.

It is worth mention that the short reaction times, easy workup, the excellent yields, and mild reaction conditions make this Knoevenagel type condensation reaction followed by cycloaddition then intramolecular exocyclic cyclization *via* addition – elimination mechanism **(**S_NAr**)**, both practical and attractive. A plausible reaction mechanism for the formation of compound **4** is shown in scheme **4**. Initially it is believed that a nucleophilic addition of an active hydrogen compound to a carbonyl group followed by a dehydration in which a molecule of water was eliminated to afford the conjugated enone **A**, which then cyclizes *via* attack NH moiety of the arylhdrazone moiety at CN, affording the pyridazinimine intermediate **B,** that was undergo intramolecular exocyclic cyclization through aromatic nucleophilic substitution reaction **(**S_NAr**)**,, which involve two steps. The first step involve addition of the nucleophile **(:NH)** to the carbon atom bearing the fluorine atom (leaving group), to yield the corresponding non-isolable Meisenheimer like complex intermediate **C**. Then the second step which furnish finally the benzo[4,5]imidazo[1,2-*b*]pyridazine derivatives **4** through elimination one molecule of HF.



Scheme 4: Plausible mechanistic pathway for the formation of benzimidazolo[1,2-*b*]pyridazine derivatives **4**.

Now it is obviously that the high electronegativity of fluorine which is the most electronegative element makes the C-F bond more dipolar and facilitates the addition of nucleophile (**:NH**) to the carbon of the aromatic ring, and this compatible with the fact that the order of reactivity for halogens in the S_NAr is F > Cl > Br > I.[37] This order clearly suggests that stronger bond dipoles associated with the more electronegative atom favor the addition step thus lowering the energy of activation of the nucleophilic addition step which is rate-determining step. Moreover the presence of electron-withdrawing groups, such as nitro group stabilizes the formed Meisenheimer complex through stabilization of the negative charge by resonance. In case of compounds **4y** and **4z** which containing fluorine atom in the *m*- position instead of the nitro

group in the *p*- position to the fluorine atom, in this case the formed negative charge in Meisenheimer complex was stabilized only inductively, not by resonance.

Conclusion

A novel green and straightforward one-pot synthesis for the benzo[4,5]imidazo[1,2-*b*]pyridazines **4a-e`** *via* intramolecular S_NAr has been developed, through the reaction of 3-oxo-2-arylhydrazonopropanals **1a-g** with 3-oxopropionitrile derivatives **2a-g**. Microwave irradiation was proved to be a superior and an efficient tool for promotion of such reactions using water as ecofriendly green solvent in the presence of sodium acetate. The X-ray crystallographic analysis was used in such investigation for the structures elucidation and regioselectivity of the reaction.

Experimental

General.

Melting points were recorded on a Griffin melting point apparatus and are reported uncorrected. IR spectra were recorded using KBr disks using a Perkin-Elmer System 2000 FT-IR spectrophotometer. ^{1}H-NMR (400 MHz) or (600 MHz) and ^{13}C-NMR (100 MHz) or (150 MHz) spectra were recorded at 25 °C using DMSO-d_6 as solvent with TMS as internal standard on a Bruker DPX 400 or 600 super-conducting NMR spectrometer. Chemical shifts are reported in ppm. Low-resolution electron impact mass spectra [MS (EI)] and High-resolution electron impact mass spectra [HRMS (EI)] were performed on high resolution GC-MS (DFS) thermo spectrometers at 70.1 eV using magnetic sector mass analyzer. Follow up of the reactions and checking homogeneity of the prepared compounds was made by thin layer chromatography (TLC). Reactions were conducted under microwave irradiation in heavy-walled Pyrex tubes fitted with PCS caps (closed vessel under pressure). Microwave heating was carried out with a

single mode cavity Explorer Microwave synthesizer (CEM Corporation, NC, USA), producing continuous irradiation and equipped with simultaneous external air-cooling system. The crystal structures were determined by a Rigaku R-AXIS RAPID diffractometer and Bruker X8 Prospector and the single crystal data collections were made by using Cu- Kα radiation. The data were collected at room temperature. The structure was solved by direct methods and was expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. The structure was solved and refined using the Bruker SHELXTL Software Package (Structure solution program- SHELXS-97 and Refinement program- SHELXL-97).[38] Data were corrected for the absorption effects using the multi-scan method (SADABS). The 3-oxopropionitrile derivatives **2c-f**, were prepared according to the literature procedures.[39,40]

General procedure for the preparation of benzimidazolo[1,2-*b*]pyridazine derivatives 4a-e`.

General method A.

Independent mixtures of 3-oxo-2-arylhydrazonopropanals **1a-g** (2 mmol), 3-oxopropionitrile derivatives **2a-g** (2 mmol), and anhydrous sodium acetate (0.25 g, 3 mmol) in water or glacial acetic acid (7 mL), The mixture was heated at refluxing temperature and the reaction was followed up by TLC and continued for 3 h (in case of H_2O) or 6 h (in case of AcOH), the separated solid products obtained on standing at room temperature were collected by filtration, washed with ethanol and recrystallized from the proper solvent, to give **4a-e**`as pure products.

General method B.

Independent mixtures of 3-oxo-2-arylhydrazonopropanals **1a-g** (2 mmol), 3-oxopropionitrile derivatives **2a-g** (2 mmol), and anhydrous sodium acetate (0.25 g, 3 mmol) in water or glacial acetic acid (7 mL), were irradiated by focused microwave using a single mode cavity explorer microwave synthesizer (CEM Corporation, NC, USA) for 10 min at 120 °C, and 250W (in case

of H_2O) or for 15 min at 125 °C, and 250W (in case of AcOH). The build-up of pressure in the closed reaction vessel was carefully monitored. After the irradiation, the reaction tube was cooled through an inbuilt system in the instrument until the temperature had fallen below 50 °C. The reaction was controlled by TLC and continued until the starting substrates were completely consumed. The solid products that formed on standing at room temperature were collected by filtration, washed with ethanol and recrystallized from the proper solvent, to give **4a-e**`as pure products.

(2-Benzoyl-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl)phenylmethanone (4a).

Recrystallized from EtOH/DMF mixture (1:2) as buff crystals, m.p. 234–235 °C; IR (KBr): ν/cm^{-1} 1675, 1659 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.61 (t, J = 8.0 Hz, 2H, Ar-H), 7.69 (t, J = 8.0 Hz, 2H, Ar-H), 7.77-7.84 (m, 2H, Ar-H), 8.04 (d, J = 8.0 Hz, 2H, Ar-H), 8.11 (d, J = 8.8 Hz, 1H, Ar-H), 8.25 (d, J = 8.0 Hz, 2H, Ar-H), 8.35 (s, 1H, pyridazine H-3), 8.46 (d, J = 8.8 Hz, 1H, Ar-H) and 8.71 ppm (d, J = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 108.83, 121.07, 121.88, 122.83, 128.65, 129.01, 129.31, 130.25, 131.05, 134.12, 134.83, 135.01, 135.05, 136.57, 142.78, 144.30, 147.28, 148.02, 189.42 and 190.62 ppm (Ar-C and CO); MS (EI): m/z (%) 423 (M^++1, 5.98), 422 (M^+, 23.25), 421 (M^+-1, 10.74); HRMS (EI): m/z Calcd. for $C_{24}H_{14}N_4O_4$ (M^+) 422.1010, found 422.1012.

2-Benzoyl-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazine-4-carboxylic acid ethyl ester (4b).

Recrystallized from dioxane/DMF mixture (1:2) as bright yellow crystals, m.p. 251–252 °C; IR (KBr): ν/cm^{-1} 1736, 1701 (2CO); ^{1}H NMR (DMSO-d_6): δ = 1.10 (t, 3H, J = 7.2 Hz, CH_3CH_2), 4.56 (q, 2H, J = 7.2 Hz, CH_3CH_2), 7.68 (t, J = 8.0 Hz, 2H, Ar-H), 7.81 (t, J = 8.0 Hz, 1H, Ar-H), 8.14-8.23 (m, 3H, Ar-H), 8.43-8.51 (m, 2H, 1 Ar-H and pyridazine H-3) and 8.85 ppm (s, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 13.68 (CH_3), 62.18 (CH_2), 108.53, 120.99, 121.67, 124.63,

128.26, 129.10, 130.56, 133.67, 134.54, 142.90, 143.06, 147.22, 147.42, 161.55, 174.79 and 188.65 ppm (Ar-C and CO); MS (EI): m/z (%) 391 (M^++1, 8.12), 390 (M^+, 34.95); HRMS (EI): m/z Calcd. for $C_{20}H_{14}N_4O_5$ (M^+) 390.0959, found 390.0958.

(2-Benzoyl-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl)(1*H*-indol-3-yl)methanone (4c). Recrystallized from EtOH/DMF mixture (1:1) as greenish yellow crystals, m.p. 299–300 °C; IR (KBr): ν/cm^{-1} 3286 (NH), 1655, 1639 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.35-7.37 (m, 2H, Ar-H), 7.57-7.59 (m, 1H, Ar-H), 7.70 (t, J = 7.6 Hz, 2H, Ar-H), 7.83 (t, J = 7.6 Hz, 1H, Ar-H), 8.12 (d, J = 9.2 Hz, 1H, Ar-H), 8.19 (s, 1H, indole H-2), 8.23 (s, 1H, pyridazine H-3), 8.26 (d, J = 7.6 Hz, 2H, Ar-H), 8.33-8.36 (m, 1H, Ar-H), 8.48 (d, J = 9.2 Hz, 1H, Ar-H), 8.88 (d, J = 2.4 Hz, 1H, Ar-H) and 12.34 ppm (s, 1H, NH); ^{13}C NMR (DMSO-*d6*): δ = 108.78, 112.64, 115.70, 121.01, 121.27, 121,61, 121.79, 122.80, 123.80, 125.36, 128.66, 129.39, 131.04, 134.09, 134.90, 137.03, 137.97, 139.23, 142.62, 145.00, 147.33, 148.39, 183.09 and 189.54 ppm (Ar-C and CO); MS (EI): m/z (%) 462 (M^++1, 15.94), 461 (M^+, 50.73); HRMS (EI): m/z Calcd. for $C_{26}H_{15}N_5O_4$ (M^+) 461.1119, found 461.1118.

(2-Benzoyl-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl)(1-methyl-1*H*-indol-3-yl)methanone (4d). Recrystallized from EtOH/DMF mixture (1:1) as pale yellow crystals, m.p. 297–298 °C; IR (KBr): ν/cm^{-1} 1662, 1643 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.80 (s, 3H, CH_3), 7.39-7.43 (m, 2H, Ar-H), 7.62-7.64 (m, 1H, Ar-H), 7.70 (t, J = 7.6 Hz, 2H, Ar-H), 7.82 (t, J = 7.6 Hz, 1H, Ar-H), 8.10 (d, J = 8.8 Hz, 1H, Ar-H), 8.18 (s, 1H, indole H-2), 8.23 (s, 1H, pyridazine H-3), 8.26 (d, J = 7.6 Hz, 2H, Ar-H), 8.33-8.35 (m, 1H, Ar-H), 8.46 (d, J = 8.8 Hz, 1H, Ar-H) and 8.87 ppm (d, J = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 33.50 (CH_3), 108.76, 111.19, 114.52, 121.05, 121.37, 121,42, 121.80, 123.19, 123.84, 125.73, 128.66, 129.33, 131.02, 134.09, 134.87, 137.76, 137.86, 142.18, 142.65, 144.81, 147.32, 148.34, 182.47 and 189.41 ppm (Ar-C and CO);

MS (EI): m/z (%) 476 (M^++1, 18.36), 475 (M^+, 71.04); HRMS (EI): m/z Calcd. for $C_{27}H_{17}N_5O_4$ (M^+) 475.1275, found 475.1275.

2-Benzoyl-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl)(1-methyl-1*H*-pyrrol-3-yl)methanone (4e). Recrystallized from EtOH/dioxane mixture (1:3) as yellow crystals, m.p. 235–236 °C; IR (KBr): ν/cm^{-1} 1660, 1639 (2CO); ^{1}H NMR (DMSO-d_6): δ = 4.09 (s, 3H, CH_3), 6.19 (d, J = 8.0 Hz, 1H, Ar-H), 6.93 (d, J = 8.0 Hz, 1H, Ar-H), 7.46 (s, 1H, Ar-H), 7.66 (t, J = 8.0 Hz, 2H, Ar-H), 7.79 (t, J = 8.0 Hz, 1H, Ar-H), 8.11 (d, J = 9.2 Hz, 1H, Ar-H), 8.16 (s, 1H, pyridazine H-3), 8.23 (d, J = 8.0 Hz, 2H, Ar-H), 8.43 (d, J = 9.2 Hz, 1H, Ar-H) and 8.80 ppm (d, J = 2.0 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 37.06 (CH_3), 108.72, 109.28, 120.96, 121.74, 125.51, 128.56, 129.16, 129.26, 129.29, 131.01, 133.99, 134.79, 134.88, 137.02, 142.59, 144.56, 147.23, 148.06, 177.82 and 189.34 ppm (Ar-C and CO); MS (EI): m/z (%) 426 (M^++1, 10.02), 425 (M^+, 41.38); HRMS (EI): m/z Calcd. for $C_{23}H_{15}N_5O_4$ (M^+) 425.1119, found 425.1118.

2-Benzoyl-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazine-4-carboxylic acid amide (4f). Recrystallized from EtOH/DMF mixture (1:2) as yellowish brown crystals, m.p. 215–216 °C; IR (KBr): ν/cm^{-1} 3309, 3145 (NH_2), 1694, 1658 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.67 (t, J = 7.6 Hz, 2H, Ar-H), 7.80 (t, J = 7.6 Hz, 1H, Ar-H), 8.19-8.22 (m, 3H, Ar-H), 8.50 (d, J = 8.8 Hz, 1H, Ar-H), 8.55 (s, 1H, pyridazine H-3), 8.80 (s, 1H, Ar-H) and 8.70, 9.06 ppm (two s, 2H, NH_2, D_2O exchangeable); ^{13}C NMR (DMSO-*d6*): δ = 109.06, 120.84, 122.33, 124.58, 128.62, 129.31, 129.58, 131.00, 134.10, 134.69, 142.97, 144.94, 146.27, 148.30, 161.24 and 189.23 ppm (Ar-C and CO); MS (EI): m/z (%) 362 (M^++1, 11.37), 361 (M^+, 48.71); HRMS (EI): m/z Calcd. for $C_{18}H_{11}N_5O_4$(M^+) 361.0806, found 361.0803.

[2-(4-Methoxybenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]phenylmethanone (4g). Recrystallized from EtOH/dioxane mixture (1:2) as yellow crystals, m.p. 216–217 °C; IR (KBr): ν/cm^{-1} 1665, 1644 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.93 (s, 3H, O*CH*$_3$), 7.20 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.60 (t, *J* = 8.0 Hz, 2H, Ar-H), 7.78 (t, *J* = 8.0 Hz, 1H, Ar-H), 8.03 (d, *J* = 8.0 Hz, 2H, Ar-H), 8.11 (d, *J* = 9.2 Hz, 1H, Ar-H), 7.27-7.29 (m, 3H, 1Ar-H and pyridazine H-3), 8.46 (d, *J* = 9.2 Hz, 1H, Ar-H) and 8.71 ppm (d, *J* = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 56.25 (O*CH*$_3$), 108.78, 109.00, 113.65, 114.71, 121.06, 123.13, 127.36, 129.01, 130.30, 133.67, 133.77, 135.09, 136.66, 142.76, 144.32, 147.25, 148.60, 164.21, 187.58 and 190.71 ppm (Ar-C and CO); MS (EI): m/z (%) 453 (M^++1, 4.65), 452 (M^+, 15.08), 451 (M^+-1, 6.52); HRMS (EI): m/z Calcd. for $C_{25}H_{16}N_4O_5$ (M^+) 452.1115, found 452.1116. Crystal Data, $C_{25}H_{16}N_4O_5$, M = 452.42, monoclinic, a = 14.2274(4) Å, b = 7.0898(2) Å, c = 21.0075(6) Å, V = 2100.02(10) Å^3, α = γ = 90°, β = 97.677(2)°, space group: P 21/c, Z = 4, D_{calc} = 1.431 g·cm^{-3} , No. of reflection measured 11409, θ_{max} = 66.15°, R1 = 0.0511 (CCDC 1425379).[41]

2-(4-Methoxybenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl-4-carboxylic acid ethyl ester (4h). Recrystallized from dioxane/DMF mixture (1:2) as yellow crystals, m.p. 217–218 °C; IR (KBr): ν/cm^{-1} 1735, 1644 (2CO); ^{1}H NMR (DMSO-d_6): δ = 1.43 (t, 3H, *J* = 7.2 Hz, *CH*$_3$CH$_2$), 3.93 (s, 3H, O*CH*$_3$), 4.54 (q, 2H, *J* = 7.2 Hz, CH$_3$*CH*$_2$), 7.20 (d, *J* = 8.8 Hz, 2H, Ar-H), 8.22-8.27 (m, 3H, Ar-H), 8.46 (s, 1H, pyridazine H-3) 8.50 (d, *J* = 9.2 Hz, 1H, Ar-H) and 8.87 ppm (d, *J* = 2.0 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 14.08 (CH$_3$), 55.73 (O*CH*$_3$), 62.52 (CH$_2$), 108.94, 114.17, 121.26, 122.00, 125.56, 127.22, 128.10, 129.34, 133.69, 142.90, 143.49, 147.44, 148.09, 161.95, 164.21 and 187.24 ppm (Ar-C and CO); MS (EI): m/z (%) 421 (M^++1, 15.33), 420 (M^+, 54.89); HRMS (EI): m/z Calcd. for $C_{21}H_{16}N_4O_6$ (M^+) 420.1064, found 420.1064.

(1*H*-Indol-3-yl)[2-(4-methoxybenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]methanone (4i). Recrystallized from EtOH/DMF mixture (1:2) as yellowish brown crystals, m.p. 285–286 °C; IR (KBr): ν/cm^{-1} 3380 (NH), 1651, 1636 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.95 (s, 3H, O*CH*$_3$), 7.22 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.34-7.36 (m, 2H, Ar-H), 7.57-7.58 (m, 1H, Ar-H), 7.96 (s, 1H, indole H-2), 8.12 (d, *J* = 9.2 Hz, 1H, Ar-H), 8.18 (s, 1H, pyridazine H-3), 8.29 (d, *J* = 8.4 Hz, 2H, Ar-H), 8.33-8.35 (m, 1H, Ar-H), 8.48 (d, *J* = 9.2 Hz, 1H, Ar-H), 8.93 (d, *J* = 2.4 Hz, 1H, Ar-H) and 12.33 ppm (s, 1H, NH); ^{13}C NMR (DMSO-*d6*): δ = 56.26 (O*CH*$_3$), 109.28, 113.10, 114.63, 116.17, 121.44, 121,75, 122.17, 122.30, 123.26, 124.25, 125.85, 127.91, 129.89, 134.12, 137.51, 138.54, 139.71, 143.07, 145.49, 147.76, 149.44, 164.63, 183.62 and 189.15 ppm (Ar-C and CO); MS (EI): m/z (%) 492 (M^++1, 11.72), 491 (M^+, 33.98); HRMS (EI): m/z Calcd. for $C_{27}H_{17}N_5O_5$ (M^+) 491.1224, found 491.1223.

[2-(4-Methoxybenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl](1-methyl-1*H*-indol-3-yl)methanone (4j). Recrystallized from EtOH/DMF mixture (1:2) as brown crystals, m.p. 283–284 °C; IR (KBr): ν/cm^{-1} 1654, 1640 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.78 (s, 3H, CH_3), 3.92 (s, 3H, O*CH*$_3$), 7.20 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.37-7.40 (m, 2H, Ar-H), 7.61-7.63 (m, 1H, Ar-H), 8.10 (d, *J* = 8.8 Hz, 1H, Ar-H), 8.14 (s, 1H, indole H-2), 8.16 (s, 1H, pyridazine H-3), 8.27 (d, *J* = 8.4 Hz, 2H, Ar-H), 8.31-8.33 (m, 1H, Ar-H), 8.45 (d, *J* = 8.8 Hz, 1H, Ar-H) and 8.87 ppm (d, *J* = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 33.95 (CH_3), 56.25 (O*CH*$_3$), 109.26, 111.66, 114.63, 114.98, 121.48, 121,83, 122.08, 122.18, 123.64, 124.29, 126.20, 127.86, 129.85, 134.10, 138.24, 138.44, 142.66, 143.10, 145.30, 147.74, 149.41, 164.63, 183.00 and 188.02 ppm (Ar-C and CO); MS (EI): m/z (%) 506 (M^++1, 13.08), 505 (M^+, 46.02); HRMS (EI): m/z Calcd. for $C_{28}H_{19}N_5O_5$ (M^+) 505.1381, found 505.1381.

[2-(4-Methoxybenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl](1-methyl-1*H*-pyrrol-3-yl)methanone (4k). Recrystallized from EtOH/dioxane mixture (1:2) as brilliant yellow crystals, m.p. 248–249 °C; IR (KBr): ν/cm^{-1} 1650, 1631 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.93 (s, 3H, CH_3), 4.09 (s, 3H, OCH_3), 6.19 (d, J = 7.2 Hz, 1H, Ar-H), 6.93 (d, J = 7.2 Hz, 1H, Ar-H), 7.18 (d, J = 8.4 Hz, 2H, Ar-H), 7.46 (s, 1H, Ar-H), 8.11 (s, 1H, pyridazine H-3), 8.13 (d, J = 9.2 Hz, 1H, Ar-H), 8.26 (d, J = 8.4 Hz, 2H, Ar-H), 8.47 (d, J = 9.2 Hz, 1H, Ar-H) and 8.89 ppm (d, J = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 36.58 (CH_3), 55.47 (OCH_3), 108.47, 108.94, 113.85, 120.69, 121.32, 121.44, 124.96, 127.26, 129.04, 129.16, 133.21, 134.42, 137.01, 142.61, 144.23, 146.99, 148.55, 163.93, 177.56 and 187.10 ppm (Ar-C and CO); MS (EI): m/z (%) 456 (M^++1, 8.91), 455 (M^+, 31.14); HRMS (EI): m/z Calcd. for $C_{24}H_{17}N_5O_5$ (M^+) 455.1224, found 455.1225.

[2-(4-Methoxybenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl](2-methyl-1*H*-indol-3-yl)methanone (4l). Recrystallized from EtOH/DMF mixture (1:2) as brown crystals, m.p. 294–295 °C; IR (KBr): ν/cm^{-1} 3392 (NH), 1658, 1634 (2CO); ^{1}H NMR (DMSO-d_6): δ = 2.36 (s, 3H, CH_3), 3.94 (s, 3H, OCH_3), 7.10 (t, J = 7.6 Hz, 1H, Ar-H), 7.18-7.21 (m, 3H, Ar-H), 7.45 (d, J = 8.0 Hz, 1H, Ar-H), 7.68 (d, J = 8.0 Hz, 1H, Ar-H), 8.10 (d, J = 8.8 Hz, 1H, Ar-H), 8.15 (s, 1H, pyridazine H-3), 8.30 (d, J = 8.4 Hz, 2H, Ar-H), 8.46 (d, J = 8.8 Hz, 1H, Ar-H), 8.93 (d, J = 2.4 Hz, 1H, Ar-H) and 12.30 ppm (s, 1H, NH); ^{13}C NMR (DMSO-*d6*): δ = 14.58 (CH_3), 55.76 (OCH_3), 109.03, 111.62, 112.31, 114.11, 120.27, 121,02, 121.21, 121.74, 122.25, 122.71, 126.80, 127.34, 129.48, 133.70, 135.12, 139.51, 142.68, 144.07, 147.30, 147.57, 149.14, 164.15, 183.34 and 187.50 ppm (Ar-C and CO); MS (EI): m/z (%) 506 (M^++1, 4.65), 505 (M^+, 13.94); HRMS (EI): m/z Calcd. for $C_{28}H_{19}N_5O_5$ (M^+) 505.1381, found 505.1379.

2-(4-Methoxybenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazine-4-carboxylic acid amide (4m). Recrystallized from EtOH/DMF mixture (1:2) as yellowish brown crystals, m.p. above 300 °C; IR (KBr): ν/cm^{-1} 3305, 3146 (NH_2), 1696, 1649 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.93 (s, 3H, OCH_3), 7.19 (d, J = 8.8 Hz, 2H, Ar-H), 8.22-8.25 (m, 3H, Ar-H), 8.51-8.54 (m, 2H, pyridazine H-3 and 1 Ar-H), 8.88 (d, J = 2.0 Hz, 1H, Ar-H) and 8.69, 9.10 ppm (two s, 2H, NH_2, D_2O exchangeable); ^{13}C NMR (DMSO-*d6*): δ = 56.26 (OCH_3), 109.58, 114.63, 121.30, 122.74, 125.29, 127.72, 129.83, 130.06, 134.13, 143.43, 145.45, 146.72, 149.33, 161.78, 164.66 and 187.86 ppm (Ar-C and CO); MS (EI): m/z (%) 392 (M^++1, 13.88), 391 (M^+, 52.78); HRMS (EI): m/z Calcd. for $C_{19}H_{13}N_5O_5$ (M^+) 391.0911, found 391.0913.

[8-Nitro-2-(4-nitrobenzoyl)benzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]phenylmethanone (4n). Recrystallized from EtOH/DMF mixture (1:3) as beige crystals, m.p. 278–279 °C; IR (KBr): ν/cm^{-1} 1674, 1652 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.61 (t, J = 7.6 Hz, 2H, Ar-H), 7.80 (t, J = 7.6 Hz, 1H, Ar-H), 8.04 (d, J = 8.0 Hz, 2H, Ar-H), 8.14 (d, J = 9.2 Hz, 1H, Ar-H), 8.43 (s, 1H, pyridazine H-3), 8.46-8.53 (m, 5H, Ar-H) and 8.91 ppm (d, J = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 108.90, 109.12, 121.18, 122.45, 122.62, 123.49, 123.59, 129.27, 130.25, 132.21, 135.03, 136.53, 140.00, 142.93, 144.27, 147.35, 147.40, 150.19, 188.42 and 190.52 ppm (Ar-C and CO); MS (EI): m/z (%) 468 (M^++1, 9.89), 467 (M^+, 34.11), 466 (M^+-1, 23.15); HRMS (EI): m/z Calcd. for $C_{24}H_{13}N_5O_6$ (M^+) 467.0860, found 467.0862.

8-Nitro-2-(4-nitrobenzoyl)benzo[4,5]imidazo[1,2-*b*]pyridazine-4-carboxylic acid ethyl ester (4o). Recrystallized from dioxane as yellow crystals, m.p. 237–238 °C; IR (KBr): ν/cm^{-1} 1731, 1677 (2CO); ^{1}H NMR (DMSO-d_6): δ = 1.44 (t, 3H, J = 7.2 Hz, CH_3CH_2), 4.55 (q, 2H, J = 7.2 Hz, CH_3CH_2), 8.25 (d, J = 9.2 Hz, 1H, Ar-H), 8.43 (d, J = 8.0 Hz, 2H, Ar-H), 8.46-8.51 (m, 3H, Ar-H), 8.54 (s, 1H, pyridazine H-3) and 8.83 ppm (d, J = 2.0 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-

d6): δ = 14.06 (CH_3), 62.61 (CH_2), 109.05, 121.37, 122.27, 123.56, 124.95, 127.97, 129.23, 132.30, 139.79, 143.08, 146.96, 147.51, 150.18, 161.80, 172.00 and 188.02 ppm (Ar-C and CO); MS (EI): m/z (%) 436 (M^++1, 6.08), 435 (M^+, 21.98); HRMS (EI): m/z Calcd. for $C_{20}H_{13}N_5O_7$ (M^+) 435.0809, found 435.0809.

(1*H*-Indol-3-yl)[8-nitro-2-(4-nitrobenzoyl)benzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]methanone (4p). Recrystallized from EtOH/DMF mixture (1:3) as bright yellowish brown crystals, m.p. above 300 °C; IR (KBr): ν/cm^{-1} 3417 (NH), 1664, 1632 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.36 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.57-7.60 (m, 1H, Ar-H), 8.13-8.17 (m, 2H, Ar-H), 8.29 (s, 1H, pyridazine H-3), 8.34-8.36 (m, 1H, Ar-H), 8.46-8.53 (m, 5H, Ar-H), 8.92 (d, *J* = 2.4 Hz, 1H, Ar-H) and 12.34 ppm (s, 1H, NH); ^{13}C NMR (DMSO-*d6*): δ = 108.84, 109.08, 115.71, 121.12, 121.24, 121,34, 123.51, 123.63, 125.35, 129.36, 132.19, 132.37, 137.05, 137.89, 139.20, 140.06, 142.79, 144.97, 147.41, 147.72, 150.18, 162.85, 182.98 and 188.53 ppm (Ar-C and CO); MS (EI): m/z (%) 507 (M^++1, 15.18), 506 (M^+, 56.04); HRMS (EI): m/z Calcd. for $C_{26}H_{14}N_6O_6$ (M^+) 506.0969, found 506.0966.

(1-Methyl-1*H*-indol-3-yl))[8-nitro-2-(4-nitrobenzoyl)benzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]methanone (4q). Recrystallized from EtOH/DMF mixture (1:3) as beige crystals, m.p. above 300 °C; IR (KBr): ν/cm^{-1} 1665, 1634 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.81 (s, 3H, CH_3), 7.41-7.44 (m, 2H, Ar-H), 7.65-7.67 (m, 1H, Ar-H), 8.15 (d, *J* = 8.8 Hz, 1H, Ar-H), 8.17 (s, 1H, indole H-2), 8.29 (s, 1H, pyridazine H-3), 8.34-8.37 (m, 1H, Ar-H), 8.47-8.54 (m, 5H, Ar-H) and 8.93 ppm (d, *J* = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 31.81 (CH_3), 108.75, 114.53, 121.18, 121.47, 122.19, 123.01, 123.65, 123.78, 125.72, 129.34, 131.36, 132.18, 132.40, 137.81, 137.86, 140.04, 142.83, 144.82, 147.42, 147.68, 150.18, 164.38, 182.40 and 188.46 ppm (Ar-C and CO);

MS (EI): m/z (%) 521 (M^++1, 23.79), 520 (M^+, 75.12); HRMS (EI): m/z Calcd. for $C_{27}H_{16}N_6O_6$ (M^+) 520.1126, found 520.1126.

(1-Methyl-1*H*-pyrrol-3-yl))[8-nitro-2-(4-nitrobenzoyl)benzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]methanone (4r). Recrystallized from EtOH/dioxane mixture (1:3) as yellow crystals, m.p. 241–242 °C; IR (KBr): ν/cm^{-1} 1674, 1636 (2CO); ^{1}H NMR (DMSO-d_6): δ = 4.09 (s, 3H, CH_3), 6.19 (d, *J* = 7.2 Hz, 1H, Ar-H), 6.92 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.47 (s, 1H, Ar-H), 8.12 (d, *J* = 9.2 Hz, 1H, Ar-H), 8.21 (s, 1H, pyridazine H-3), 8.43-8.49 (m, 5H, Ar-H) and 8.84 ppm (d, *J* = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 37.07 (CH_3), 108.92, 109.31, 121.09, 121.41, 121.99, 123.52, 125.50, 129.17, 129.26, 132.28, 134.95, 136.97, 139.99, 142.79, 144.55, 147.32, 147.46, 150.11, 177.71 and 188.36 ppm (Ar-C and CO); MS (EI): m/z (%) 471 (M^++1, 13.81), 470 (M^+, 51.22); HRMS (EI): m/z Calcd. for $C_{23}H_{14}N_6O_6$(M^+) 470.0969, found 470.0966.

(2-Methyl-1*H*-indol-3-yl))[8-nitro-2-(4-nitrobenzoyl)benzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]methanone (4s). Recrystallized from EtOH/DMF mixture (1:2) as brown crystals, m.p. 219–220 °C; IR (KBr): ν/cm^{-1} 3372 (NH), 1673, 1636 (2CO); ^{1}H NMR (DMSO-d_6): δ = 2.36 (s, 3H, CH_3), 7.08 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.18 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.44 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.67 (d, *J* = 8.0 Hz, 1H, Ar-H), 8.10 (d, *J* = 8.8 Hz, 1H, Ar-H), 8.25 (s, 1H, pyridazine H-3), 8.44-8.49 (m, 5H, Ar-H), 8.90 (d, *J* = 2.4 Hz, 1H, Ar-H) and 12.31 ppm (s, 1H, NH); ^{13}C NMR (DMSO-*d6*): δ = 14.57 (CH_3), 109.13, 111.63, 112.32, 120.26, 121,16, 122.03, 122.26, 122.73, 123.46, 126.78, 129.38, 132.39, 135.14, 139.47, 140.04, 142.87, 144.04, 145.84, 147.41, 147.67, 147.93, 150.09, 183.19 and 188.28 ppm (Ar-C and CO); MS (EI): m/z (%) 521 (M^++1, 11.05), 520 (M^+, 35.18); HRMS (EI): m/z Calcd. for $C_{27}H_{16}N_6O_6$ (M^+) 520.1126, found 520.1124.

8-Nitro-2-(4-nitrobenzoyl)benzo[4,5]imidazo[1,2-*b*]pyridazine-4-carboxylic acid amide(4t). Recrystallized from dioxane/DMF mixture (1:1) as brown crystals, m.p. 295–296 °C; IR (KBr): ν/cm^{-1} 3331, 3173 (NH_2), 1704, 1675 (2CO); ^{1}H NMR (DMSO-d_6): δ = 8.23 (d, J = 9.2 Hz, 1H, Ar-H), 8.42 (d, J = 8.4 Hz, 2H, Ar-H), 8.46-8.53 (m, 3H, Ar-H), 8.60 (s, 1H, pyridazine H-3), 8.86 (d, J = 2.4 Hz, 1H, Ar-H) and 8.71, 9.05 ppm (two s, 2H, NH_2, D_2O exchangeable); ^{13}C NMR (DMSO-*d6*): δ = 109.15, 120.90, 122.49, 123.52, 124.22, 129.16, 129.41, 132.26, 139.74, 143.09, 144.74, 146.25, 147.68, 150.12, 161.05 and 188.05 ppm (Ar-C and CO); MS (EI): m/z (%) 407 (M^++1, 17.45), 406 (M^+, 100); HRMS (EI): m/z Calcd. for $C_{18}H_{10}N_6O_6$ (M^+) 406.0656, found 406.0652.

[2-(4-Bromobenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]phenylmethanone (4u). Recrystallized from DMSO as yellow crystals, m.p. above 300 °C; IR (KBr): ν/cm^{-1} 1663, 1640 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.61 (t, J = 8.0 Hz, 2H, Ar-H), 7.79 (t, J = 8.0 Hz, 1H, Ar-H), 7.94 (d, J = 8.4 Hz, 2H, Ar-H), 8.04 (d, J = 8.0 Hz, 2H, Ar-H), 8.14 (d, J = 8.8 Hz, 1H, Ar-H), 8.21 (d, J = 8.4 Hz, 2H, Ar-H), 8.37 (s, 1H, pyridazine H-3), 8.49 (d, J = 8.8 Hz, 1H, Ar-H) and 8.94 ppm (d, J = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 108.96, 109.52, 121.09, 121.95, 122.74, 128.43, 129.01, 129.30, 130.23, 131.78, 132.97, 133.87, 135.04, 136.56, 142.86, 144.19, 147.29, 147.74, 188.50 and 190.57 ppm (Ar-C and CO); MS (EI): m/z (%) 502 (M^++2, 29.98), 501 (M^++1, 20.18), 500 (M^+, 28.42), 499 (M^+-1, 12.08); HRMS (EI): m/z Calcd. for $C_{24}H_{13}{}^{79}BrN_4O_4$ (M^+) 500.0115, found 500.0115. Crystal Data, moiety formula: $C_{24}H_{13}BrN_4O_4$, C_2H_6OS, sum formula: $C_{26}H_{19}BrN_4O_5S$, M = 579.41, triclinic, a = 6.6551(11) Å, b = 14.067(2) Å, c = 14.367(2) Å, V = 1239.2(4) Å^3, α = 106.520(11)°, β = 100.524(12)°, γ = 98.459(11)°, space group: P-1, Z = 2, D_{calc} = 1.553 g·cm^{-3}, No. of reflection measured 13412, θ_{max} = 66.74°, R1 = 0.0486 (CCDC 1420059).[41]

2-(4-Bromobenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazine-4-carboxylic acid ethyl ester (4v). Recrystallized from EtOH/DMF mixture (1:2) as yellow crystals, m.p. 210–211 °C; IR (KBr): ν/cm^{-1} 1737, 1704 (2CO); ^{1}H NMR (DMSO-d_6): δ = 1.44 (t, 3H, J = 7.2 Hz, CH_3CH_2), 4.54 (q, 2H, J = 7.2 Hz, CH_3CH_2), 7.90 (d, J = 7.6 Hz, 2H, Ar-H), 8.16 (d, J = 7.6 Hz, 2H, Ar-H), 8.25 (d, J = 8.8 Hz, 1H, Ar-H), 8.49-8.52 (m, 2H, 1 Ar-H and pyridazine H-3) and 8.87 ppm (s, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 14.06 (CH_3), 62.56 (CH_2), 109.02, 121.30, 122.14, 125.20, 127.99, 128.44, 129.26, 131.76, 132.94, 133.69, 143.00, 143.37, 147.26, 147.46, 161.85 and 188.13 ppm (Ar-C and CO); MS (EI): m/z (%) 470 (M^++2, 37.05), 469 (M^++1, 10.12), 468 (M^+, 36.53); HRMS (EI): m/z Calcd. for $C_{20}H_{13}{}^{79}BrN_4O_5$ (M^+) 468.0064, found 468.0063.

[2-(4-Bromobenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl](1*H*-Indol-3-yl)methanone (4w). Recrystallized from DMSO as yellow crystals, m.p. above 300 °C; IR (KBr): ν/cm^{-1} 3342 (NH), 1660, 1638 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.34-7.37 (m, 2H, Ar-H), 7.57 (d, J = 8.0 Hz, 1H, Ar-H), 7.93 (d, J = 8.4 Hz, 2H, Ar-H), 8.13 (d, J = 9.2 Hz, 1H, Ar-H), 8.16 (s, 1H, indole H-2), 8.20 (d, J = 8.4 Hz, 2H, Ar-H), 8.22 (s, 1H, pyridazine H-3), 8.34 (d, J = 8.0 Hz, 1H, Ar-H), 8.49 (d, J = 9.2 Hz, 1H, Ar-H), 8.93 (d, J = 2.4 Hz, 1H, Ar-H) and 12.36 ppm (s, 1H, NH); ^{13}C NMR (DMSO-*d6*): δ = 108.93, 112.16, 115.70, 121.58, 122.86, 122.95, 125.37, 128.41, 129.40, 131.88, 132.90, 133.94, 137.06, 137.97, 139.40, 140.85, 142.72, 143.94, 145.00, 147.36, 148.11, 162.79, 183.05 and 189.64 ppm (Ar-C and CO); MS (EI): m/z (%) 541 (M^++2, 12.95), 540 (M^++1, 4.01), 539 (M^+, 12.16); HRMS (EI): m/z Calcd. for $C_{26}H_{14}{}^{79}BrN_5O_4$ (M^+) 539.0224, found 539.0224. Crystal Data, moiety formula: $C_{26}H_{14}BrN_5O_4$, C_2H_6OS, sum formula: $C_{28}H_{20}BrN_5O_5S$, M = 618.45, monoclinic, a = 17.8147(8) Å, b = 7.4508(5) Å, c = 21.5768(11)

Å, V = 2718.0(3) Å^3, α = γ = 90°, β = 108.369(3)°, space group: P 21/n, Z = 4, D_{calc} = 1.511 g·cm^{-3} , No. of reflection measured 16961, θ_{max} = 66.62°, R1 = 0.0444 (CCDC 1420055).[41]

[2-(4-Bromobenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl](1-methyl-1*H*-indol-3-yl)methanone (4x). Recrystallized from EtOH/DMF mixture (1:2) as brown crystals, m.p. 280–281 °C; IR (KBr): ν/cm^{-1} 1659, 1636 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.80 (s, 3H, CH_3), 7.41 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.63 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.92 (d, *J* = 8.4 Hz, 2H, Ar-H), 8.12 (d, *J* = 9.2 Hz, 1H, Ar-H), 8.16 (s, 1H, indole H-2), 8.20 (d, *J* = 8.4 Hz, 2H, Ar-H), 8.21 (s, 1H, pyridazine H-3), 8.33 (d, *J* = 7.6 Hz, 1H, Ar-H), 8.47 (d, *J* = 9.2 Hz, 1H, Ar-H) and 8.93 ppm (d, *J* = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 33.53 (CH_3), 108.94, 111.25, 114.54, 121.11, 121,35, 121.39, 121.92, 123.24, 123.89, 125.74, 128.45, 129.37, 131.83, 132.97, 133.92, 137.80, 137.88, 142.21, 142.76, 144.83, 147.37, 148.06, 182.48 and 188.53 ppm (Ar-C and CO); MS (EI): m/z (%) 555 (M^++2, 48.71), 554 (M^++1, 16.05), 553 (M^+, 46.29); HRMS (EI): m/z Calcd. for $C_{27}H_{16}{}^{79}BrN_5O_4$ (M^+) 553.0380, found 553.0379.

[2-(4-Bromobenzoyl)-7-fluorobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl](1*H*-Indol-3-yl)methanone (4y). Recrystallized from EtOH/DMF mixture (1:2) as yellowish brown crystals, m.p. above 300 °C; IR (KBr): ν/cm^{-1} 3245 (NH), 1661, 1632 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.34-7.36 (m, 2H, Ar-H), 7.44 (t, *J* = 9.2 Hz, 1H, Ar-H-8), 7.56 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.76 (d, *J* = 9.2 Hz, 1H, Ar-H-9), 7.90 (d, *J* = 7.6 Hz, 2H, Ar-H), 8.10 (s, 1H, indole H-2), 8.14 (s, 1H, pyridazine H-3), 8.17-8.25 (m, 3H, Ar-H), 8.35 (d, *J* = 8.0 Hz, 1H, Ar-H) and 12.31 ppm (s, 1H, NH); ^{13}C NMR (DMSO-*d6*): δ = 105.62 (d, $^2J_{CF}$ = 24 Hz), 112.40 (d, $^2J_{CF}$ = 26 Hz), 112.60, 113.63 (d, $^3J_{CF}$ = 10 Hz), 115.71, 119.19, 121.27, 122.73, 123.72, 125.39, 126.89, 128.02, 131.66, 132.93, 134.27, 137.01, 137.23, 139.05, 141.97, 144.47 (d, $^3J_{CF}$ = 16 Hz), 146.92, 161.29 (d, $^1J_{CF}$ = 241 Hz), 183.66 and 188.84 ppm (Ar-C and CO); MS (EI): m/z (%) 514 (M^++2,

39.02), 513 (M^++1, 14.16), 512 (M^+, 38.14); HRMS (EI): m/z Calcd. for $C_{26}H_{14}{}^{79}BrFN_4O_2(M^+)$ 512.0279, found 512.0278. Crystal Data, moiety formula: $C_{26}H_{14}BrFN_4O_2$, M = 513.31, monoclinic, a = 14.361(6) Å, b = 14.051(6) Å, c = 11.274(4) Å, V = 2158(2) $Å^3$, α = γ = 90°, β = 108.430(7)°, space group: P 21/c, Z = 4, D_{calc} = 1.580 $g \cdot cm^{-3}$, No. of reflection measured 4380, θ max = 26.37°, R1 = 0.0388 (CCDC 1420056).[41]

[2-(4-Bromobenzoyl)-7-fluorobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl](1-methyl-1*H*-indol-3-yl)methanone (4z). Recrystallized from EtOH/DMF mixture (1:2) as beige crystals, m.p. 280–281 °C; IR (KBr): ν/cm^{-1} 1666, 1638 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.80 (s, 3H, CH_3), 7.37-7.46 (m, 3H, Ar-H), 7.63 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.76 (d, *J* = 9.6 Hz, 1H, Ar-H9), 7.90 (d, *J* = 8.4 Hz, 2H, Ar-H), 8.09 (s, 1H, indole H-2), 8.15 (s, 1H, pyridazine H-3), 8.17-8.25 (m, 3H, Ar-H) and 8.34 ppm (d, *J* = 8.0 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 33.53 (CH_3), 105.72 (d, $^2J_{CF}$ = 25 Hz), 111.24, 112.60 (d, $^2J_{CF}$ = 29 Hz), 113.70 (d, $^3J_{CF}$ = 12 Hz), 114.62, 119.08, 121.47, 123.24, 123.90, 125.84, 126.94, 128.13, 131.74, 132.99, 134.30, 137.20, 137.84, 141.85, 142.12, 144.55 (d, $^3J_{CF}$ = 13 Hz), 146.96, 161.40 (d, $^1J_{CF}$ = 240 Hz), 183.17 and 188.80 ppm (Ar-C and CO); MS (EI): m/z (%) 528 (M^++2, 41.35), 527 (M^++1, 13.85), 526 (M^+, 38.98); HRMS (EI): m/z Calcd. for $C_{27}H_{16}{}^{79}BrFN_4O_2$ (M^+) 526.0435, found 526.0436.

[2-(4-chlorobenzoyl)-8-nitrobenzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl](1*H*-Indol-3-yl)methanone (4a`). Recrystallized from EtOH/DMF mixture (1:2) as pale brown crystals, m.p. 299–300 °C; IR (KBr): ν/cm^{-1} 3391 (NH), 1655, 1634 (2CO),; ^{1}H NMR (DMSO-d_6): δ = 7.34-7.36 (m, 2H, Ar-H), 7.57 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.78 (d, *J* = 8.4 Hz, 2H, Ar-H), 8.11-816 (m, 2H, 1Ar-H and indole H-2), 8.22 (s, 1H, pyridazine H-3), 8.28 (d, *J* = 8.4 Hz, 2H, Ar-H), 8.34 (d, *J* = 7.6 Hz, 1H, Ar-H), 8.49 (d, *J* = 9.2 Hz, 1H, Ar-H), 8.92 (d, *J* = 2.0 Hz, 1H, Ar-H) and 12.34 ppm (s, 1H, NH); ^{13}C NMR (DMSO-*d6*): δ = 109.36, 113.10, 116.14, 121.49, 121.72, 121.98, 122.32,

123.28, 124.28, 125.80, 129.31, 129.83, 133.36, 134.05, 137.49, 138.38, 139.56, 139.66, 143.15, 145.43, 147.80, 148.56, 183.50 and 188.87 ppm (Ar-C and CO); MS (EI): m/z (%) 496 (M^++1, 3.84), 495 (M^+, 12.46); HRMS (EI): m/z Calcd. for $C_{26}H_{14}ClN_5O_4$(M^+) 495.0729, found 495.0729,

(1*H*-Indol-3-yl)[8-nitro-2-(thiophene-2-carbonyl)benzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]-methanone (4b`). Recrystallized from EtOH/DMF mixture (1:3) as yellow crystals, m.p. above 300 °C; IR (KBr): ν/cm^{-1} 3407 (NH), 1648, 1633 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.35-7.56 (m, 4H, Ar-H), 8.11-8.23 (m, 3H, Ar-H), 8.33-8.57 (m, 4H, Ar-H), 9.10 (s, 1H, Ar-H) and 12.32 ppm (s, 1H, NH); ^{13}C NMR (DMSO-*d6*): δ = 109.00, 112.61, 114.48, 115.66, 120.77, 121.10, 121,30, 121.94, 122.78, 123.81, 125.35, 129.09, 129.41, 137.02, 138.00, 138.11, 138.38, 139.23, 142.80, 145.00, 147.40 147.80, 179.62 and 183.00 ppm (Ar-C and CO); MS (EI): m/z (%) 468 (M^++1, 13.42), 467 (M^+, 44.95); HRMS (EI): m/z Calcd. for $C_{24}H_{13}N_5O_4S$ (M^+) 467.0683, found 467.0683.

(1-Methyl-1*H*-indol-3-yl))[8-nitro-2-(thiophene-2-carbonyl)benzo[4,5]imidazo[1,2-*b*]pyrid-azin-4-yl]methanone (4c'). Recrystallized from EtOH/DMF mixture (1:2) as yellow crystals, m.p. above 300 °C; IR (KBr): ν/cm^{-1} 1650, 1633 (2CO); ^{1}H NMR (DMSO-d_6): δ = 3.81 (s, 3H, CH_3), 7.40-7.42 (m, 2H, Ar-H), 7.47 (t, J = 6.6 Hz, 1H, Ar-H), 7.63 (d, J = 8.4 Hz, 1H, Ar-H), 8.14 (d, J = 9.0 Hz, 1H, Ar-H), 8.15 (s, 1H, indole H-2), 8.22 (s, 1H, pyridazine H-3), 8.32 (d, J = 6.6 Hz, 1H, Ar-H), 8.35 (d, J = 8.4 Hz, 1H, Ar-H), 8.50 (d, J = 9.0 Hz, 1H, Ar-H), 8.57 (t, J = 6.6 Hz, 1H, Ar-H) and 9.13 ppm (d, J = 2.4 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 33.17 (CH_3), 108.71, 110.83, 114.35, 120.23, 120.95, 121.18, 121.66, 122.87, 123.57, 125.60, 128.75, 129.21, 137.61, 137.67, 137.82, 137.98, 138.65, 141.80, 142.79, 144.54, 147.19, 147.66, 179.29

and 182.03 ppm (Ar-C and CO); MS (EI): m/z (%) 482 (M^++1, 21.59), 481 (M^+, 83.40); HRMS (EI): m/z Calcd. for $C_{25}H_{15}N_5O_4S$ (M^+) 481.0839, found 481.0838.

(1-Methyl-1*H*-pyrrol-3-yl))[8-nitro-2-(thiophene-2-carbonyl)benzo[4,5]imidazo[1,2-*b*]pyridazin-4-yl]methanone (4d'). Recrystallized from dioxane as yellow crystals, m.p. 282–283 °C; IR (KBr): ν/cm^{-1} 1655, 1638 (2CO); ^{1}H NMR (DMSO-d_6): δ = 4.09 (s, 3H, CH_3), 7.47 (t, J = 6.0 Hz, 1H, Ar-H), 6.91 (d, J = 6.0 Hz, 1H, Ar-H), 7.46-7.48 (m, 2H, Ar-H), 8.16 (d, J = 9.2 Hz, 1H, Ar-H), 8.19 (s, 1H, pyridazine H-3), 8.34 (d, J = 6.4 Hz, 1H, Ar-H), 8.51 (d, J = 9.2 Hz, 1H, Ar-H), 8.57 (t, J = 6.4 Hz, 1H, Ar-H) and 9.10 ppm (d, J = 2.0 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-*d6*): δ = 37.06 (CH_3), 109.04, 109.31, 120.93, 121.11, 121.96, 125.55, 129.09, 129.17, 129.38, 134.90, 137.14, 138.17, 138.34, 138.83, 142.83, 144.64, 147.34, 147.61, 177.78 and 179.56 ppm (Ar-C and CO); MS (EI): m/z (%) 432 (M^++1, 12.30), 431 (M^+, 53.19); HRMS (EI): m/z Calcd. for $C_{21}H_{13}N_5O_4S$ (M^+) 431.0683, found 431.0682.

8-nitro-2-(thiophene-2-carbonyl)benzo[4,5]imidazo[1,2-*b*]pyridazine-4-carboxylic acid amide (4e'). Recrystallized from dioxane/DMF mixture (1:2) as yellowish brown crystals, m.p. above 300 °C; IR (KBr): ν/cm^{-1} 3335, 3152 (NH_2), 1701, 1649 (2CO); ^{1}H NMR (DMSO-d_6): δ = 7.47 (t, J = 5.6 Hz, 1H, Ar-H), 8.28 (d, J = 8.8 Hz, 1H, Ar-H), 8.35 (d, J = 5.6 Hz, 1H, Ar-H), 8.57-8.58 (m, 2H, Ar-H), 8.62 (s, 1H, pyridazine H5), 8.11 (s, 1H, Ar-H) and 8.72, 9.10 ppm (two s, 2H, NH_2, D_2O exchangeable); ^{13}C NMR (DMSO-*d6*): δ = 109.34, 120.16, 120.95, 122.51, 127.60, 129.18, 135.06, 136.35, 137.70, 138.27, 139.69, 144.05, 44.98, 161.20, 178.84 and 179.41 ppm (Ar-C and CO); MS (EI): m/z (%) 368 (M^++1, 11.23), 367 (M^+, 65.79); HRMS (EI): m/z Calcd. for $C_{16}H_9N_5O_4S$ (M^+) 367.0370, found 367.0370.

Acknowledgements

Financial support for this study was provided by the University of Kuwait through a research grant (SC14/13). The facilities of Analab/SAF supported by research grants GS01/01, GS01/05, GS01/03 and GS03/08 are gratefully acknowledged.

Supporting Information

- CheckCIF files for the x-ray crystallographic data for four compounds are given.
- Proton and carbon NMR spectra for newly characterized compounds.

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