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ARTICLE

An Approach towards the Synthesis of Novel Fused Nitrogen Tricyclic Heterocyclic Scaffolds via GBB Reaction

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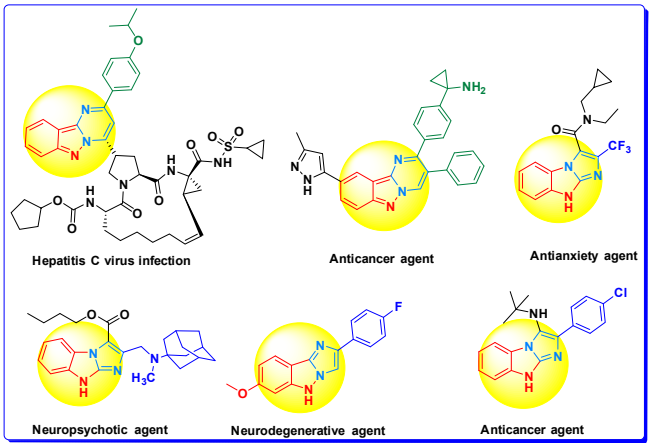
A concise and efficient one-pot synthesis of novel *N*-fused tricyclic derivatives has been developed by using Groebke-Blackburn-Bienayme (GBB) reaction, which involved the reaction of 3-amino-1*H*-indazoles, aldehydes and isonitriles to afford 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amine derivatives *via* [4+1] formal cycloaddition reaction. Furthermore, we describe an unprecedented reaction of chromone-3-carboxaldehydes with 3-amino-1*H*-indazoles to afford (2-hydroxyphenyl)(pyrimido[1,2-*b*]indazol-3-yl)methanones in one-pot at ambient temperature. This protocol features, robust method for one-step construction of new tricyclic rings, column chromatography free methods with clean reaction profile, high yields, operational simplicity and tolerate a diverse collection of reactants.

1. Introduction

In the family of heterocyclic compounds Nitrogen-fused bi- and tri-cyclic scaffolds have received substantial attention in drug discovery and development programs.[1] The compounds containing nitrogen prodigiously occur in natural products and synthetic drugs. Indeed the synthetic drugs widely contain more number nitrogen atoms than the natural products because nitrogen can bear a positive charge, and act as a hydrogen bond donor and/or acceptor that substantially influences the interaction between the drug with the biochemical structure of the target.[2] In addition, p*K*a values of amines are in the span of physiological pH, an important factor that influences the pharmacokinetics properties of the drugs.[3] Therefore, the development of novel nitrogen-rich heterocyclic compounds is highly desirable. More specifically fused imidazo-indazole[4] systems have shown promise in a majority of therapeutic areas due to their pronounced biological activity.[5] These heterocycles are adaptable chemical building blocks for use in both a 'drug hunter's probe to discover new lead molecules and a biologists search for potent molecular tools. The recent drug discovery and development process have authenticated the discovery of new methodologies which rapidly have enabled access to a broad spectrum of these basic chemo-types. Such adamant chemo-types, all containing a bridgehead nitrogen atom,[6] are thus poised for an ever increasing impact on the discovery and development of new chemical entities (NCEs). The wide spectrum of biological features of these frameworks, such as anticancer activity by inhibition of topoisomerase IIα,[7] antianxiety,[8] neuropsychotic[9] activities, and also used to treat hepatitis C virus (HCV) infection.[10] They are cognitive enhancers effective in the treatment of several neurodegenerative diseases, including familial Alzheimer's Disease and Down's syndrome[11] (Scheme 1).



Scheme 1. Pharmaceutically important imidazo[1,2-*b*]indazole and pyrimido[1,2-*b*]indazole derivatives.

In addition, these scaffolds allow the efficient creation of functionally diverse molecules for the further discovery of novel, biologically interesting molecules.[12] Therefore, the development of efficient synthetic approaches toward such scaffolds is instrumental in the rapid synthesis and evaluation of these compounds. Unfortunately, owing to their importance and utility, no

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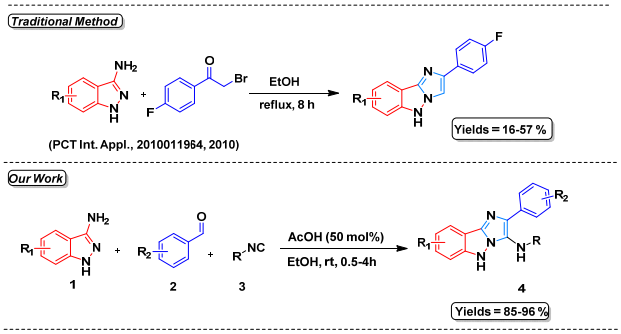
considerable attention has been paid to construct tricyclic 2-aryl-5*H*-imidazo[1,2-*b*]indazole derivatives. The existing patent method has their own drawbacks, including use of expensive reagents, limited structural diversity of the product, harsh reaction conditions, low yields and use of α-halo carbonyl compounds which have lachrymatory properties.[11]



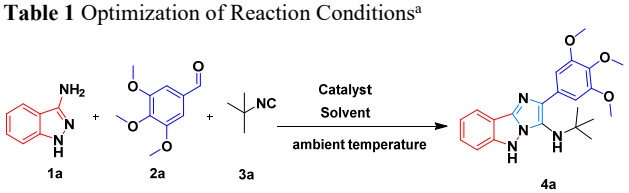
Scheme 2. One-pot three-component synthesis of 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amines (**4**).

Initially, to access the tricyclic 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amines, the inspiration was derived from the Groebke–Blackburn–Bienayme three-component reaction (GBB-3CR).[13] The three-component Ugi-variant (Ugi-3CR) GBB reaction was discovered independently by three research groups, Katrin Groebke,[13a] Christopher Blackburn[13b] and Hugues Bienayme [13c] in 1998. This reaction consists of a heterocyclic amine, an aldehyde and an isocyanide that proceeds through imine formation and subsequent formal [4+1] cycloaddition to form structurally diverse and highly substituted, drug-like heterocyclic libraries. Indeed, the GBB reaction is a highly competent example of an isocyanide-based multicomponent reaction (IMCR).[14] Therefore, the further development of new GBB-based eco-friendly methodologies is highly desirable.[12c, 13e, 13g] The IMCRs represent a family of versatile organic molecules that bear unique electronic properties and have been extensively applied in synthetic organic chemistry, particularly in the synthesis of nitrogen-containing molecules and drug-like products with potential bioactivities.[15] Similarly, isocyanide-based [4+1] cycloaddition reactions[16] have been widely used, owing to the ability of isocyanides to act as electrophiles as well as nucleophiles. Indeed, the formal [4+1] cycloaddition reactions are a powerful tool for the rapid construction of diverse heterocycles which are found in central core of many natural products and synthetic libraries.[17] Given our interest in the development of novel MCRs[18] and new molecular diversity via subsequent product manipulation and fascinated by the medicinal profile of these pharmacophores, we envisioned a one-pot IMCR to afford a suite of novel 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amine scaffolds via formal [4+1] cycloaddition reaction. To the best of our knowledge, this is the first example for the construction of tricyclic 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amine derivatives (Scheme 2).

2. Results and discussion

The reaction conditions were optimized using 3-amino-1*H*-indazole (**1a**, 1 mmol), 3,4,5-trimethoxybenzaldehyde (**2a**, 1 mmol), and *tert*-butyl isocyanide (**3a**, 1 mmol), as the model substrates (Scheme 2). At the outset, these three reactants were dissolved in EtOH and allowed it to stir at room temperature in the absence of any catalyst for 12 h. After 12 h (the reaction was monitored by TLC), we could not observe any product formation (Table 1, entry 1). Next, the same set of reaction was performed in the presence of p-TsOH, we were pleased to find that with 20 mol % *p*-TsOH, this reaction afforded the desired product **4a** in 57% yield. (Table 1, entry 2). The structure of **4a**, was assigned with the help of ^{1}H NMR, ^{13}C NMR, and HRMS data. Encouraged by this result, we evaluated the use of several different acids to further optimize the reaction conditions. The other acids, including $Sc(OTf)_3$, TFA, TfOH, $HClO_4$, and AcOH, were screened, and the results of these experiments are summarized in Table 1 (entries 3-7). Among all the screened catalysts acetic acid was found superior with respect to reaction time and product yield (Table 1, entry 7). Moreover, we found that the yields were obviously affected by the amount of acetic acid loaded. The yield of **4a**, was increased appreciably, when 50 mol%, of acetic acid was used (Table 1, entry 8). Furthermore, no significant improvement in the reaction rate and product yield was observed while increasing the amount of catalyst loading (Table 1, entry 9). At this juncture, solvents representing other categories such as polar aprotic (THF, CH_3CN), nonpolar (toluene), polar protic (MeOH, H_2O), and halogenated ($CHCl_3$), were screened (Table 1, entries 10–15). Among the various solvent tested, a drop in the yield was observed in the case of polar aprotic and nonpolar solvents (Table 1, entries 11-13). Notably, all the reactants remained unconsumed when water is used as solvent (Table 1, entry 15). The results revealed that ethanol is the optimal solvent for this reaction (Table 1, entry 8). We were pleased to achieve complete conversion of reactant and high yield of the **4a** using 50 mol% of acetic acid in ethanol at ambient temperature for 2h. Similarly, we also investigated the scope of L-proline as a catalyst for the same set reaction (Table 1, entries 14-15). Interestingly, 20 mol % of L-proline also catalyze the reaction and afforded the desired product **4a** in optimum yield with sparingly slower rates (Table 1, entry 15). It is particularly advantageous; since the products were solid and could be collected by simple filtration avoiding conventional chromatographic purification.

Table 1 Optimization of Reaction Conditions[a]



Entry	Catalyst (mol %)	Solvent	Time (h)	Yield[b] (%)
1	-	EtOH	12	-[c]
2	*p*-TsOH (20)	EtOH	12	57

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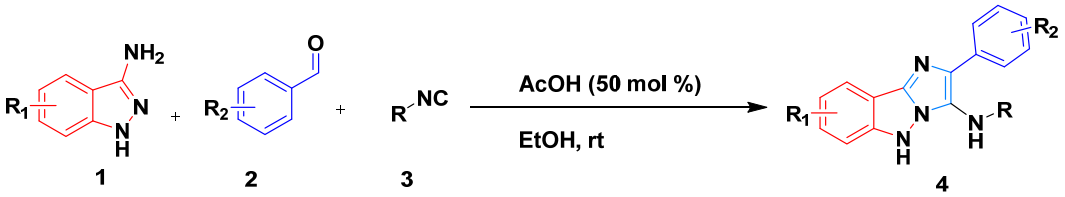
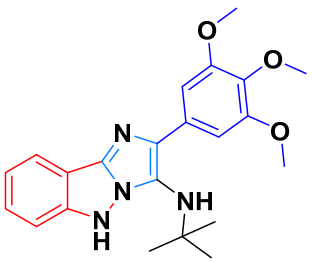
3	$Sc(OTf)_3$ (20)	EtOH	12	48[d]
4	TFA (20)	EtOH	12	42
5	TfOH (20)	EtOH	12	49
6	$HClO_4$ (20)	EtOH	12	63
7	AcOH (20)	EtOH	4	87
8	**AcOH (50)**	**EtOH**	**2**	**96**
9	AcOH (100)	EtOH	2	92
10	AcOH (50)	$CHCl_3$	4	83
11	AcOH (50)	CH_3CN	4	76
12	AcOH (50)	THF	4	63
13	AcOH (50)	toluene	4	56
14	AcOH (50)	MeOH	4	85
15	AcOH(50)	H_2O	4	-[c]
16	L-proline (10)	EtOH	12	78[d]
17	L-proline (20)	EtOH	12	81

[a]Reaction Conditions: 1.0 mmol of **1a**, 1.0 mmol of **2a**, and 1.0 mmol **3a**, in presence of catalyst in 2.5 ml of solvent (including the other solvents tested). Ambient temperature, [b]Isolated yield, [c]No Reaction, [d]Reactants remained unconsumed.

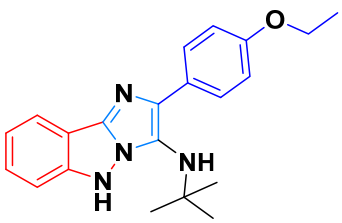
Having optimized reaction conditions, we proceeded to expand the scope of the reaction with a broad array of aromatic aldehyde substrates (Table 2). A series of aldehydes with electron-donating and electron-withdrawing substituents on the phenyl ring (e.g. -Me, -OMe, -OEt, -Cl) underwent the desired transformation in a regiospecific fashion to deliver the corresponding products (**4a–4ab**) in good to excellent yields (**85–96%**). The electronic and steric properties of the aromatic aldehyde substrate had very little impact on the efficiency of this reaction. The phenyl ring was replaced by a naphthalene moiety (**4e**) in good yield of the product as expected. Similarly, trans-cinnamaldehyde was also suitable for this reaction (**4s**). We were delighted to find that the heteroaryl aldehydes such as, thiophene-2-carboxaldehyde, and furan-2-carboxaldehyde afforded the desired products in good yields without affecting the heterocyclic moieties (**4t, 4u, 4v**). Next, we investigated the scope of this reaction for aliphatic aldehydes such as cyclohexanecarboxaldehyde and butyraldehyde; however reaction did not proceed (**4ac** and **4ad**). Further diversity in the products was introduced by using other isocyanides substrates, although no specific electronic effect on the reaction yield was observed when *tert*-butyl isocyanide and cyclohexyl isocyanide were subjected to reaction, afforded the desired products in good to excellent yields. However, aromatic isocyanide derivatives such as 4-methoxyphenyl isocyanide were unable to proceed with the reaction. We also employed substituted 3-amino-1*H*-indazoles such as (–F and –Br), are tolerated well, and provided a corresponding products in good to excellent yields under the optimized reaction condition. Therefore, the present protocol has general applicability, accommodating a variety of substitution patterns.

Table 2 Substrate Scope[a,b]

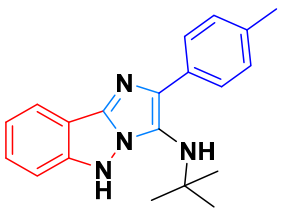




4a (1.5 h; 96%)



4b (1.5 h; 94%)



4c (0.5 h; 91%)

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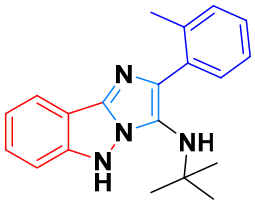
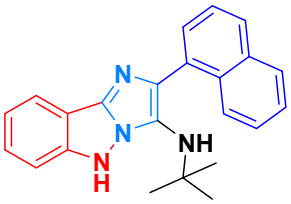
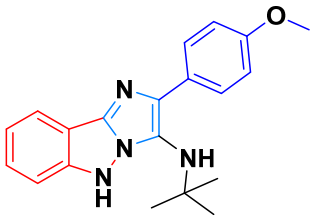


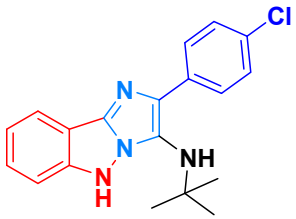
4d (1 h; 88%)



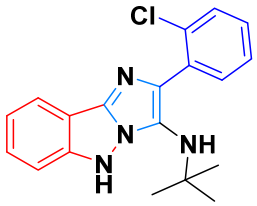
4e (2 h; 90%)



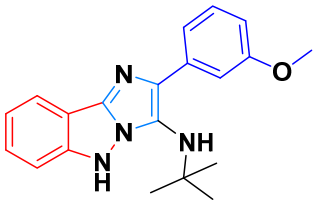
4f (1.2 h; 94%)



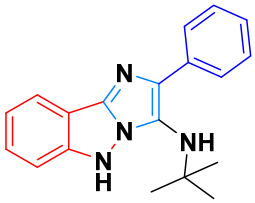
4g (2.5 h; 87%)



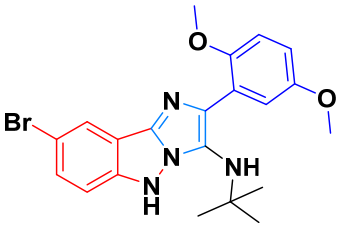
4h (3 h; 85%)



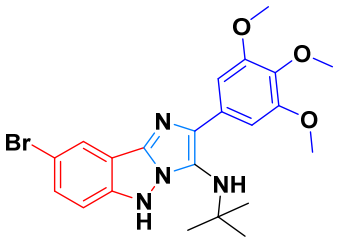
4i (1.5 h; 93%)



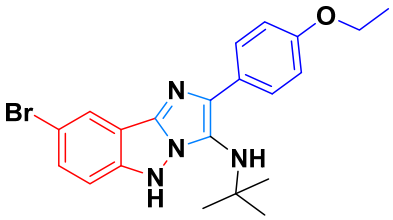
4j (0.5 h; 96%)



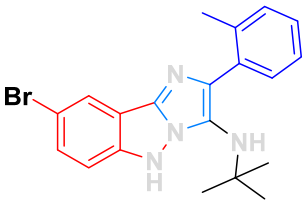
4k (2.2 h; 94%)



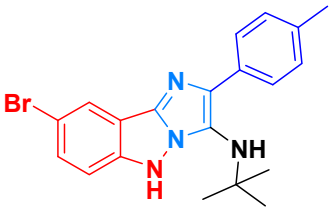
4l (2 h; 95%)



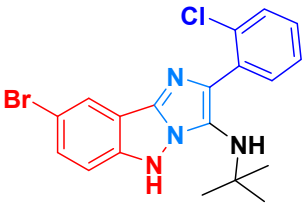
4m (1.5 h; 88%)



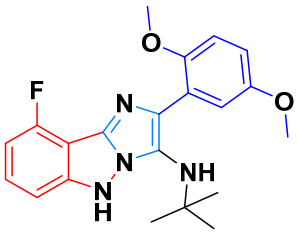
4n (1.5 h; 86%)



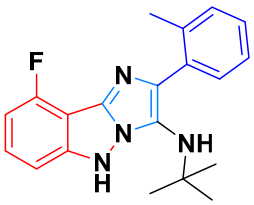
4o (1.5 h; 91%)



4p (3.2 h; 86%)



4q (2.5 h; 92%)



4r (2 h; 90%)

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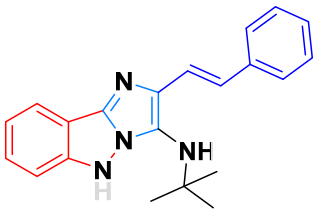
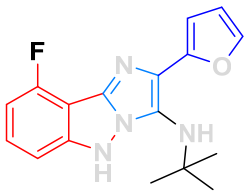
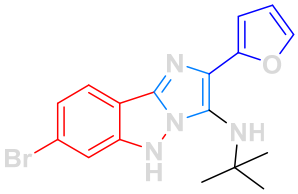


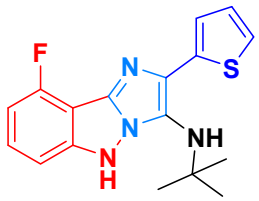
4s (4 h; 95%)



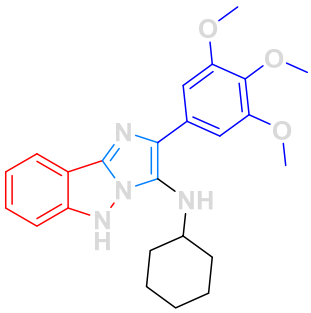
4t (4 h; 88%)



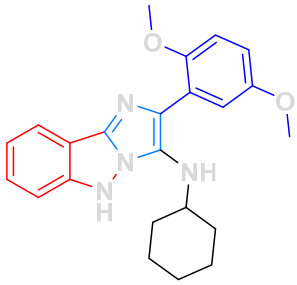
4u (3.8 h; 85%)



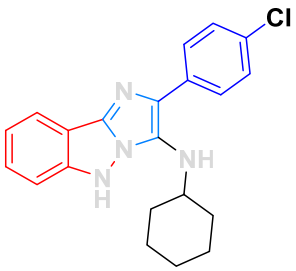
4v (4 h, 89%)



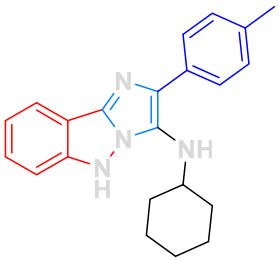
4w (1.5 h; 94%)



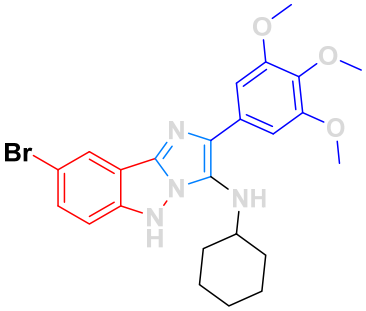
4x (1.5 h; 89%)



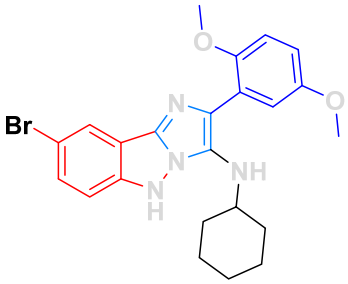
4y (1.5 h; 91%)



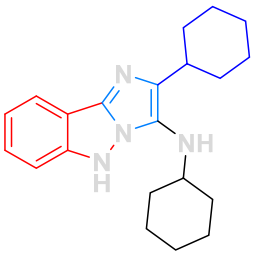
4z (1.5 h; 88%)



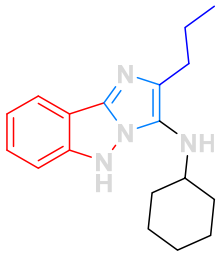
4aa (1.5 h; 92%)



4ab (1.5 h; 90%)



4ac (4 h; 0%)



4ad (4 h; 0%)

[a]Reactions were performed with **1** (1 mmol), **2** (1 mmol) and **3** (1 mmol), in the presence of 50 mol % acetic acid in 2.5 mL ethanol at ambient temperature, [b]Isolated yields.

All the structure of synthesized compounds (**4a-4ab**) have been ascertained on the basis of ^{1}H NMR, ^{13}C NMR and HRMS data.

After having successfully developed one-pot strategy for the synthesis of diverse 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amines via one-pot GBB reaction, we envisaged to examine the synthetic utility of this reaction. Consequently, we have performed the reaction on a gram-scale (10 mmol, 1.33g) under the standard conditions and isolated the desired product **4a** in 88% yield (Scheme 3).

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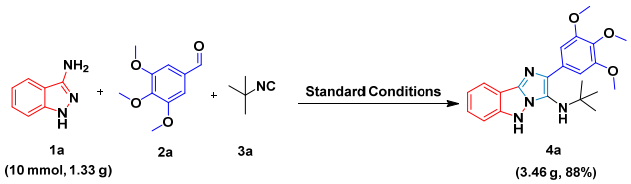
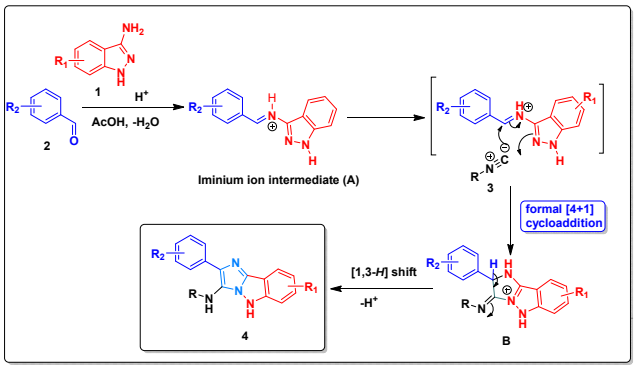


Scheme 3 Gram Scale Reaction.

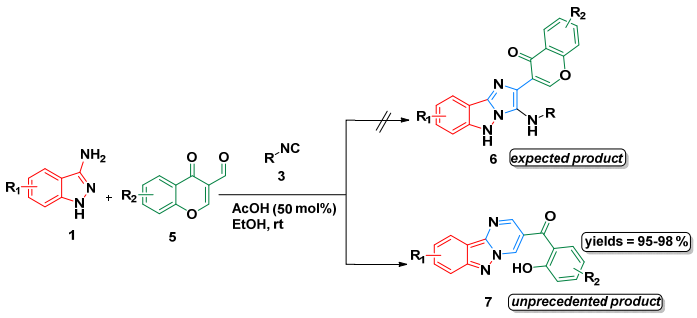
Based on our experimental results and literature reports [13a, 13e] we have proposed a possible mechanism for the formation of 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amines (**4**) in Scheme 4.



Scheme 4. Possible reaction mechanism for the synthesis of 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amines (**4**).

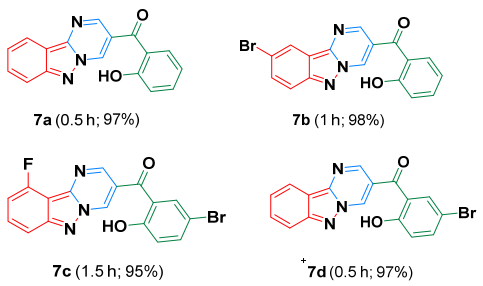
Initially, the reaction of 3-amino-1*H*-indazole (**1**) and benzaldehyde (**2**) occurs to give iminium ion intermediate **A**, which on formal [4 + 1] cycloaddition with *tert*-butylisocyanide (**3**) yields nitrilium ion intermediate **B**, which on rearomatization followed by 1,3-*H* shift, afforded the desired product (**4**) in good to excellent yields.

During the course of our investigations on the synthesis of densely functionalized 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amines, the reaction of 3-amino-1*H*-indazole with chromone-3-carboxaldehyde (**5**) and *tert*-butylisocyanide which was expected to afford 3-(3-(*tert*-butylamino)-5*H*-imidazo[1,2-*b*]indazol-2-yl)-4H-chromen-4-one (**6**), surprisingly we observed an unprecedented product, (2-hydroxyphenyl) (pyrimido[1,2-*b*]indazol-3-yl)methanone (**7**) under identical reaction conditions (Scheme 5). The literature scan revealed that, there are few reports described the successful implantation of a GBB reaction using chromone-3-carboxaldehyde.[19] While this chromone-3-carboxaldehyde moiety have three electrophilic centers in their structure could react by different reactive modes with various nucleophiles leading to ring-opening/ring-closure to afford novel heterocyclic scaffolds.[20] Notably, the reaction of chromone-3-carboxaldehyde with electron-rich amino heterocycles such as 3-amino-1*H*-indazole afforded fused (2-hydroxyphenyl) (pyrimido[1,2-*b*]indazol-3-yl)methanones and the substrate scope is given in Table 3.



Scheme 5. Unprecedented formation of (2-hydroxyphenyl)(pyrimido[1,2-*b*]indazol-3-yl)methanone (**7**).

Table 3 Substrate Scope[a,b]



[a]Reaction conditions: **1a** (1 mmol), **5a** (1mmol) and acetic acid (50 mol %), in 3 mL ethanol at ambient temperature, [b]Isolated yields.

3. Conclusion

In summary, we have developed a highly efficient approach for the synthesis of *N*-rich novel tricyclic heterocycles *via* efficient use of Groebke-Blackburn-Bienayme reaction. In addition, we successfully achieved the synthesis of (2-hydroxyphenyl) (pyrimido[1,2-*b*]indazol-3-yl) methanones in one-pot with good yields. This synthetic approach has various prominent features such as shorter reaction times, simplicity in operation, skeletal diversity, and scalability with excellent yields. This protocol obviates tedious work-up and purifications techniques such as column chromatography for the isolation of the products which makes this protocol cost-effective and environmentally friendly. We believe that, these features will facilitate this procedure to find extensive applications in the field of organic and medicinal chemistry.

4. Experimental

4.1 Material and methods

Chemicals were purchased from Aldrich and Alfa Aesar Chemical Companies and used without further purification. NMR spectra were recorded in parts per million (ppm) in DMSO-d_6 on a Jeol JNM ECP 600 NMR instrument using TMS as internal standard. Standard abbreviations were used to denote signal multiplicities (s = singlet,

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d = doublet, t = triplet, q = quartet, m = multiplet). HRMS were obtained by EI on a double-focusing mass analyzer, ESI (positive ion mode) on TOF mass analyzer. All melting points were determined using open capillaries on an Electrothermal-9100 (Japan) instrument and are uncorrected. The elemental analysis (C, H, and N) was performed using an Elementar Analysensysteme GmbH.

4.2 Typical experimental procedure for the Synthesis of 2-aryl-5*H*-imidazo[1,2-*b*]indazol-3-amines.

To a mixture of 3-amino-1*H*-indazoles (**1**, 1 mmol), aldehydes (**2**, 1 mmol) and isocyanides (**3**, 1 mmol), in 2.5 ml of ethanol was added acetic acid (50 mol %) and the reaction mixture was stirred at ambient temperature, the progress of the reaction was monitored by TLC (7:3 EtOAc/Hexane; R_f = 0.28). After completion of the reaction, solid products was filtered under vacuum, air dried, triturated and washed with chloroform: ethanol (80:20, v/v) to obtain the analytically pure products. The compounds **4a-4ab** were also synthesized by adopting this procedure.

4.3 Typical experimental procedure for the Synthesis of (2-hydroxyphenyl)(pyrimido[1,2-*b*]indazol-3-yl)methanones.

A mixture of 3-amino-1*H*-indazoles (**1**, 1 mmol) and chromone-3-carboxaldehydes (**5**, 1 mmol) in 3 ml of ethanol was added acetic acid (50 mol %) and reaction mixture was stirred at room temperature, the progress of the reaction was monitored by TLC. After completion of the reaction, solid products was filtered under vacuum and air dried to obtain the analytically pure products.

***N*-(*tert*-butyl)-2-(3,4,5-trimethoxyphenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4a)**. Yield: 96 % (378.4 mg); White solid; Mp: 246-248 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.34 (s, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.50 (s, 2H), 7.44 (d, *J* = 8.7 Hz, 1H), 7.23 – 7.15 (m, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 4.50 (s, 1H), 3.88 (s, 6H), 3.71 (s, 3H), 1.20 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 152.89, 151.57, 136.82, 131.35, 131.28, 126.32, 124.99, 124.47, 121.35, 118.46, 115.58, 114.67, 103.64, 103.42, 60.17, 56.04, 55.06, 30.45.; HRMS (ESI, m/z): calcd for $C_{22}H_{26}N_4O_3$ (M+H$^+$) 394.2005, found: 394.2007. Anal. Calcd: C, 66.99; H, 6.64; N, 14.20. Found: C, 66.50; H, 6.75; N, 14.43.

***N*-(*tert*-butyl)-2-(4-ethoxyphenyl)-5H-imidazo[1,2-*b*]indazol-3-amine (4b).** Yield: 94% (326.7 mg); White solid; Mp: 242-244 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.28 (s, 1H), 8.01 (d, *J* = 8.9 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 8.7 Hz, 1H), 7.22 – 7.14 (m, 1H), 7.03 (d, *J* = 8.7 Hz, 2H), 6.83 (t, *J* = 7.3 Hz, 1H), 4.34 (s, 1H), 4.06 (q, *J* = 7.0 Hz, 2H), 1.34 (t, *J* = 7.0 Hz, 3H), 1.13 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 157.87, 151.38, 131.20, 127.71, 124.75, 123.20, 120.60, 118.46, 115.38, 114.57, 114.35, 103.59, 63.07, 55.08, 30.29, 14.69; HRMS (ESI, m/z): calcd for $C_{21}H_{24}N_4O$ (M+H$^+$) 348.1950, found: 348.1946. Anal. Calcd: C, 72.39; H, 6.94; N, 16.08. Found: C, 71.94; H, 6.85; N, 16.31.

***N*-(*tert*-butyl)-2-(p-tolyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4c).** Yield: 91 % (289.6 mg); Off White solid; Mp: 248-250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.31 (s, 1H), 7.99 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.21 – 7.16 (m, 1H), 6.83 (t, *J* = 7.4 Hz, 1H), 4.39 (s, 1H), 2.34 (s, 3H), 1.13 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 151.49, 136.73, 131.39, 129.08, 128.09, 126.16, 124.89, 124.65, 121.18, 118.55, 115.42, 114.59, 103.52, 55.18, 30.30, 20.86.; HRMS (ESI, m/z): calcd for $C_{20}H_{22}N_4$ (M+H$^+$) 318.1844, found: 318.1838. Anal. Calcd: C, 75.44; H, 6.96; N, 17.60. Found: C, 75.03; H, 7.03; N, 17.85.

***N*-(*tert*-butyl)-2-(o-tolyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4d).** Yield: 88 % (280.6 mg); White solid; Mp: 246-248 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.21 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.38 – 7.28 (m, 3H), 7.19 (t, *J* = 7.3 Hz, 1H), 6.82 (t, *J* = 7.2 Hz, 1H), 4.15 (s, 1H), 2.40 (s, 3H), 0.96 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 151.74, 137.59, 132.01, 131.60, 130.90, 130.82, 129.08, 126.19, 125.32, 124.84, 122.25, 118.87, 115.78, 115.07, 104.12, 55.12, 30.48, 20.68.; HRMS (ESI, m/z): calcd for $C_{20}H_{22}N_4$ (M+H$^+$) 318.1844, found: 318.1839. Anal. Calcd: C, 75.44; H, 6.96; N, 17.60. Found: C, 74.98; H, 7.09; N, 17.71.

***N*-(*tert*-butyl)-2-(naphthalen-1-yl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4e).** Yield: 90 % (318.4 mg); White solid; Mp: 227-229 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.49 (s, 1H), 8.12 – 7.97 (m, 3H), 7.81 (d, *J* = 6.8 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.62 – 7.56 (m, 2H), 7.49 (d, *J* = 8.6 Hz, 1H), 7.26 – 7.19 (m, 1H), 6.91–6.80 (m, 1H), 4.20 (s, 1H), 0.89 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 133.38, 131.47, 129.35, 129.33, 128.92, 128.39, 126.72, 126.13, 125.87, 125.46, 124.96, 122.68, 119.92, 118.51, 115.39, 114.61, 79.22, 54.52, 29.86.; HRMS (ESI, m/z): calcd for $C_{23}H_{22}N_4$ (M+H$^+$) 354.1844, found: 354.1847. Anal. Calcd: C, 77.94; H, 6.26; N, 15.81. Found: C, 77.62; H, 6.39; N, 16.04.

***N*-(*tert*-butyl)-2-(4-methoxyphenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4f).** Yield: 94 % (314.1 mg); Pale pink solid; Mp: 234-236 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.58 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.09 – 7.04 (m, 2H), 4.58 (s, 1H), 3.82 (s, 3H), 1.11 (s, 9H); ^{13}C

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{^{1}H} NMR (150 MHz, DMSO- d_6) δ 158.99, 145.51, 137.78, 131.67, 128.15, 128.12, 126.15, 125.52, 122.48, 121.31, 119.07, 114.07, 113.59, 105.38, 55.34, 55.24, 30.05.; HRMS (ESI, m/z): calcd for $C_{20}H_{22}N_4O$ (M+H$^+$) 334.1794, found: 334.1791. Anal. Calcd: C, 71.83; H, 6.63; N, 16.75. Found: C, 71.53; H, 6.74; N, 16.98.

***N*-(*tert*-butyl)-2-(4-chlorophenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4g).** Yield: 87 % (295.7 mg); Off white solid; Mp: 216-218 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.88 (s, 1H), 8.11 (d, *J* = 8.6 Hz, 2H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.57 (d, *J* = 8.6 Hz, 2H), 7.51 – 7.47 (m, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 4.61 (s, 1H), 1.13 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 145.55, 137.77, 132.37, 132.10, 129.63, 128.64, 128.14, 128.12, 126.47, 126.46, 125.52, 124.87, 122.37, 119.02, 113.95, 55.52, 30.11.; HRMS (ESI, m/z): calcd for $C_{19}H_{19}ClN_4$ (M+H$^+$) 338.1298, found: 338.1295. Anal. Calcd: C, 67.35; H, 5.65; N, 16.54. Found: C, 66.98; H, 5.79; N, 16.26.

***N*-(*tert*-butyl)-2-(2-chlorophenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4h).** Yield: 85 % (287.2 mg); White solid; Mp: 215-217 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 13.00 (s, 1H), 8.19 (s, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.40 – 7.28 (m, 2H), 7.07 – 6.98 (m, 1H), 4.69 (s, 1H), 1.10 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 146.05, 138.27, 132.87, 132.60, 130.13, 129.14, 128.63, 128.62, 126.98, 126.02, 122.87, 119.51, 114.45, 56.01, 30.60.; HRMS (ESI, m/z): calcd for $C_{19}H_{19}ClN_4$ (M+H$^+$) 338.1298, found: 338.1296. Anal. Calcd: C, 67.35; H, 5.65; N, 16.54. Found: C, 67.03; H, 5.85; N, 16.31.

***N*-(*tert*-butyl)-2-(3-methoxyphenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4i).** Yield: 93 % (310.8 mg); Pale pink solid; Mp: 221-224 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.37 (s, 1H), 7.77 – 7.72 (m, 2H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 8.7 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.0 Hz, 1H), 6.84 (t, *J* = 7.3 Hz, 1H), 4.47 (s, 1H), 3.84 (s, 3H), 1.16 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 159.30, 151.64, 139.19, 132.19, 131.55, 129.62, 125.07, 124.29, 121.74, 119.85, 119.63, 118.63, 118.43, 115.52, 114.64, 113.15, 111.50, 103.44, 57.73, 55.21, 30.35.;HRMS (ESI, m/z): calcd for $C_{20}H_{22}N_4O$ (M+H$^+$) 334.1794, found: 334.1789. Anal. Calcd: C, 71.83; H, 6.63; N, 16.75. Found: C, 71.51; H, 6.91; N, 17.04.

***N*-(*tert*-butyl)-2-phenyl-5*H*-imidazo[1,2-*b*]indazol-3-amine (4j).** Yield: 96 % (291.9 mg); Pale pink solid; Mp: 240-242 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.50 (s, 1H), 8.43 (s, 1H), 8.10 (d, *J* = 7.1 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.53 – 7.42 (m, 4H), 7.21 (s, 1H), 6.90 – 6.79 (m, 1H), 4.59 (s, 1H), 1.17 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 151.80, 133.20, 131.90, 130.67, 129.84, 128.42, 125.29, 124.70, 122.87, 122.31, 121.92, 118.69, 115.70, 114.71, 103.36, 55.34, 30.31.; HRMS (ESI, m/z): calcd for $C_{19}H_{20}N_4$ (M+H$^+$) 304.1688, found: 304.1683. Anal. Calcd: C, 74.97; H, 6.62; N, 18.41. Found: C, 74.67; H, 6.73; N, 18.69.

8-Bromo-*N*-(*tert*-butyl)-2-(2,5-dimethoxyphenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4k). Yield: 94 % (416.7 mg); off White solid; Mp: 244-246 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.98 (s, 1H), 7.93 (s, 1H), 7.54 (s, 1H), 7.41 (d, *J* = 8.9 Hz, 1H), 7.25 (d, *J* = 8.9 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 1H), 6.98 (d, *J* = 8.5 Hz, 1H), 4.15 (s, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 1.04 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 153.11, 150.12, 149.74, 141.08, 130.79, 127.56, 122.41, 120.84, 119.64, 116.62, 115.66, 114.71, 113.17, 56.32, 55.58, 54.86, 29.96.; HRMS (ESI, m/z): calcd for $C_{21}H_{23}BrN_4O_2$ (M+H$^+$) 442.1004, found: 442.1008. Anal. Calcd: C, 56.89; H, 5.23; N, 12.64. Found: C, 57.09; H, 5.47; N, 12.41.

8-bromo-*N*-(*tert*-butyl)-2-(3,4,5-trimethoxyphenyl)-5H-imidazo[1,2-*b*]indazol-3-amine (4l). Yield: 95 % (448.3 mg); White solid; Mp: 240-242 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.57 – 10.79 (m, 1H), 7.87 (s, 1H), 7.47 (s, 2H), 7.41 (d, *J* = 8.9 Hz, 1H), 7.26 (d, *J* = 8.9 Hz, 1H), 4.54 (s, 1H), 3.88 (s, 6H), 3.71 (s, 3H), 1.18 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 161.32, 153.19, 152.91, 149.77, 140.20, 136.99, 130.53, 129.30, 127.65, 126.09, 121.44, 120.50, 116.76, 106.84, 105.58, 103.78, 60.18, 56.06, 55.95, 55.02, 30.41.; HRMS (ESI, m/z): calcd for $C_{22}H_{25}BrN_4O_3$ (M+H$^+$) 472.1110, found: 472.1116. Anal. Calcd: C, 55.82; H, 5.32; N, 11.84. Found: C, 55.91; H, 5.38; N, 12.04.

8-bromo-*N*-(*tert*-butyl)-2-(4-ethoxyphenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4m). Yield: 88 % (374.9 mg); White solid; Mp: 215-217 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 12.54 (s, 1H), 7.96 (d, *J* = 7.3 Hz, 2H), 7.85 (s, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.29 (d, *J* = 9.0 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 2H), 4.44 (s, 1H), 4.07 (q, 2H), 1.34 (t, *J* = 6.5 Hz, 3H), 1.10 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 158.16, 148.96, 130.41, 127.94, 125.80, 122.65, 120.90, 120.52, 116.46, 114.44, 107.40, 105.33, 63.12, 55.13, 30.19, 14.68.; HRMS (ESI, m/z): calcd for $C_{21}H_{23}BrN_4O$ (M+H$^+$) 426.1055, found: 426.1057.

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Anal. Calcd: C, 59.02; H, 5.43; N, 13.11. Found: C, 58.94; H, 5.68; N, 13.19.

8-bromo-*N*-(*tert*-butyl)-2-(o-tolyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4n). Yield: 86 % (341.0 mg); White solid; Mp: 230-232 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 12.32 (s, 1H), 7.81 (s, 1H), 7.54 (d, *J* = 7.3 Hz, 1H), 7.43 (d, J = 9.1 Hz, 1H), 7.36 (d, *J* = 3.3 Hz, 2H), 7.34 – 7.29 (m, 1H), 7.26 (d, *J* = 9.0 Hz, 1H), 4.21 (s, 1H), 2.38 (s, 3H), 0.95 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 149.51, 137.13, 131.09, 130.64, 130.36, 130.09, 128.76, 127.50, 125.73, 125.09, 121.92, 120.33, 116.74, 106.54, 104.85, 54.59, 29.96, 20.12.. HRMS (ESI, m/z): calcd for $C_{20}H_{21}BrN_4$ (M+H$^+$) 396.0950, found: 396.0954. Anal. Calcd: C, 60.46; H, 5.33; N, 14.10. Found: C, 60.58; H, 5.47; N, 14.34.

8-bromo-*N*-(*tert*-butyl)-2-(p-tolyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4o). Yield: 91 % (360.2 mg); Off White solid; Mp: 244-245 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 12.56 (s, 1H), 7.95 (d, *J* = 6.7 Hz, 2H), 7.86 (s, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.32 – 7.27 (m, 3H), 4.48 (s, 1H), 2.34 (s, 3H), 1.11 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 149.23, 137.17, 130.64, 129.26, 127.96, 127.67, 126.34, 125.65, 121.43, 120.58, 116.55, 107.37, 105.20, 55.22, 30.21, 20.88..; HRMS (ESI, m/z): calcd for $C_{20}H_{21}BrN_4$ (M+H$^+$) 396.0950, found: 396.0954. Anal. Calcd: C, 60.46; H, 5.33; N, 14.10. Found: C, 60.38; H, 5.51; N, 14.36.

8-bromo-N-(*tert*-butyl)-2-(2-chlorophenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4p). Yield: 86 % (358.1 mg); White solid; Mp: 223-225 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 12.32 (s, 1H), 7.85 (s, 1H), 7.74 (d, *J* = 7.1 Hz, 1H), 7.64 (d, *J* = 7.4 Hz, 1H), 7.51 – 7.47 (m, 2H), 7.44 (d, *J* = 10.0 Hz, 1H), 7.28 (d, *J* = 9.1 Hz, 1H), 4.16 (s, 1H), 0.97 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 158.33, 149.71, 134.72, 133.24, 133.19, 133.06, 130.63, 130.52, 130.20, 129.80, 128.21, 127.78, 127.75, 127.27, 122.74, 120.51, 116.76, 106.72, 54.57, 29.83.; HRMS (ESI, m/z): calcd for $C_{19}H_{18}BrClN_4$ (M+H$^+$) 416.0403, found: 416.0407. Anal. Calcd: C, 54.63; H, 4.34; N, 13.41. Found: C, 54.38; H, 4.43; N, 13.46.

***N*-(*tert*-butyl)-2-(2,5-dimethoxyphenyl)-9-fluoro-5*H*-imidazo[1,2-*b*]indazol-3-amine (4q).** Yield: 92 % (351.5 mg); Off white solid; Mp: 243-245 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 12.35 (s, 1H), 7.24 (d, *J* = 7.4 Hz, 2H), 7.17 – 7.08 (m, 2H), 7.00 (d, *J* = 8.9 Hz, 1H), 6.54 (t, *J* = 8.8 Hz, 1H), 3.99 (s, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 1.00 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 155.64, 153.99, 153.12, 150.31, 141.27, 129.38, 125.22, 125.16, 122.83, 119.83, 116.48, 114.90, 113.11, 110.79, 109.77, 56.32, 55.59, 54.72, 29.86.; HRMS (ESI, m/z): calcd for $C_{21}H_{23}FN_4O_2$ (M+H$^+$) 382.1805, found: 382.1809. Anal. Calcd: C, 65.95; H, 6.06; N, 14.65. Found: C, 66.05; H, 6.26; N, 14.73.

***N*-(*tert*-butyl)-9-fluoro-2-(o-tolyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4r).** Yield: 90 % (303.0 mg); White solid; Mp: 238-240 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 13.05 (s, 1H), 7.56 – 7.46 (m, 1H), 7.36 – 7.24 (m, 5H), 6.77 – 6.63 (m, 1H), 4.40 (s, 1H), 2.34 (s, 3H), 0.91 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 160.41, 160.00, 155.52, 153.86, 151.22, 151.19, 142.16, 137.54, 131.40, 130.30, 129.34, 129.11, 129.01, 127.11, 126.23, 125.69, 122.57, 109.98, 101.39, 101.29, 95.36, 95.23, 54.78, 29.79, 20.04.; HRMS (ESI, m/z): calcd for $C_{20}H_{21}FN_4$(M+H$^+$) 336.1750, found: 336.1754. Anal. Calcd: C, 71.41; H, 6.29; N, 16.65. Found: C, 71.12; H, 6.38; N, 16.43.

(*E*)-*N*-(*tert*-butyl)-2-styryl-5*H*-imidazo[1,2-*b*]indazol-3-amine (4s). Yield: 95 % (314.1 mg); Brown solid; Mp: 235-237 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 12.32 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 7.4 Hz, 2H), 7.44 – 7.38 (m, 3H), 7.32 – 7.25 (m, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.08 (d, *J* = 16.5 Hz, 1H), 6.83 (t, *J* = 7.2 Hz, 1H), 4.72 (s, 1H), 1.25 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 151.96, 136.99, 132.64, 129.17, 128.97, 128.13, 127.47, 125.96, 125.27, 125.11, 124.40, 123.86, 118.59, 116.40, 115.64, 114.73, 102.99, 79.21, 54.78, 30.07.;HRMS (ESI, m/z): calcd for $C_{21}H_{22}N_4$ (M+H$^+$) 330.1844, found: 330.1846. Anal. Calcd: C, 76.33; H, 6.71; N, 16.96. Found: C, 75.93; H, 6.78; N, 17.04.

***N*-(*tert*-butyl)-9-fluoro-2-(furan-2-yl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4t).** Yield: 88 % (275.0 mg); Off White solid; Mp: 233-235 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.51 (s, 1H), 7.82 (s, 1H), 7.23 (d, *J* = 8.6 Hz, 1H), 7.14 (m, 1H), 7.02 (s, 1H), 6.66 (m, 1H), 6.59 – 6.53 (m, 1H), 4.48 (s, 1H), 1.22 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 155.63, 153.99, 144.80, 142.42, 125.54, 125.53, 125.49, 125.48, 121.67, 111.78, 110.82, 110.80, 110.79, 107.48, 79.21, 54.94, 30.22.; HRMS (ESI, m/z): calcd for $C_{17}H_{17}FN_4O$ (M+H$^+$) 312.1386, found: 312.1389. Anal. Calcd: C, 65.37; H, 5.49; N, 17.94. Found: C, 65.03; H, 5.63; N, 18.04.

7-bromo-N-(*tert*-butyl)-2-(furan-2-yl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4u). Yield: 85 % (316.0 mg); White solid; Mp: 241-243 °C; ^{1}H

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NMR (600 MHz, DMSO- d_6) δ 12.21 (s, 1H), 7.92 (d, *J* = 7.4 Hz, 2H), 7.48 (s, 2H), 7.10 (d, *J* = 2.7 Hz, 1H), 6.71 (dd, *J* = 3.3, 1.7 Hz, 1H), 4.71 (s, 1H), 1.22 (s, 9H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO- d_6) δ 157.23, 143.71, 142.99, 131.42, 127.40, 121.87, 121.21, 115.80, 115.78, 112.16, 108.28, 99.51, 55.65, 30.07.; HRMS (ESI, m/z): calcd for $C_{17}H_{17}BrN_4O$ ($M+H^+$) 372.0586, found: 372.0588. Anal. Calcd: C, 54.59; H, 4.63; N, 15.01. Found: C, 54.70; H, 4.59; N, 15.29.

***N*-(*tert*-butyl)-9-fluoro-2-(thiophen-2-yl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4v).** Yield: 89 % (292.0 mg); White solid; Mp: 225-227 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 12.26 (s, 1H), δ 7.75 (d, *J* = 3.3 Hz, 1H), 7.56 (d, *J* = 4.9 Hz, 1H), 7.24 (d, *J* = 8.6 Hz, 1H), 7.17 – 7.11 (m, 2H), 6.62 – 6.55 (m, 1H), 4.50 (s, 1H), 1.28 (s, 9H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO- d_6) δ 155.88, 155.63, 153.99, 138.44, 133.86, 131.04, 128.32, 126.73, 126.35, 125.44, 125.39, 124.71, 120.79, 110.91, 54.66, 30.46.; HRMS (ESI, m/z): calcd for $C_{17}H_{17}FN_4S$ ($M+H^+$) 328.1158, found: 328.1161. Anal. Calcd: C, 62.17; H, 5.22; N, 17.06. Found: C, 62.03; H, 5.41; N, 17.36.

***N*-cyclohexyl-2-(3,4,5-trimethoxyphenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4w).** Yield: 94 % (394.8 mg); Off White solid; Mp: 217-219 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 12.30 (s, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 8.9 Hz, 3H), 7.23 – 7.18 (m, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 4.78 (d, *J* = 5.5 Hz, 1H), 3.89 (s, 6H), 3.71 (s, 3H), 3.62 – 3.49 (m, 1H), 1.85 – 1.78 (m, 2H), 1.71 – 1.65 (m, 2H), 1.54 – 1.49 (m, 1H), 1.35 – 1.27 (m, 2H), 1.22 – 1.13 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO- d_6) δ 153.07, 151.94, 136.53, 131.27, 126.04, 125.17, 122.77, 121.08, 118.53, 115.69, 114.60, 103.44, 102.80, 60.17, 55.98, 53.91, 51.03, 33.30, 25.61, 24.20.; HRMS (ESI, m/z): calcd for $C_{24}H_{28}N_4O_3$ ($M+H^+$) 420.2161, found: 420.2167. Anal. Calcd: C, 68.55; H, 6.71; N, 13.32. Found: C, 68.39; H, 6.78; N, 13.43.

***N*-cyclohexyl-2-(2,5-dimethoxyphenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4x).** Yield: 89 % (347.0 mg); Off White solid; Mp: 214-216 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 11.92 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.45 – 7.40 (m, 2H), 7.21 – 7.17 (m, 1H), 7.11 (d, *J* = 9.1 Hz, 1H), 6.96 – 6.93 (m, 1H), 6.83 – 6.79 (m, 1H), 4.47 (d, *J* = 8.0 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.66 – 3.57 (m, 1H), 1.81 – 1.73 (m, 2H), 1.62 – 1.55 (m, 2H), 1.51 – 1.42 (m, 1H), 1.19 – 1.10 (m, 5H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO- d_6) δ 153.24, 151.96, 149.79, 131.81, 125.10, 124.04, 119.75, 118.95, 115.29, 115.19, 114.98, 114.34, 113.96, 113.25, 103.39, 56.29, 55.52, 52.76, 33.22, 25.49, 24.21; HRMS (ESI, m/z): calcd for $C_{23}H_{26}N_4O_2$ ($M+H^+$) 390.2056, found: 390.2051. Anal. Calcd: C, 70.75; H, 6.71; N, 14.35. Found: C, 70.45; H, 6.93; N, 14.46.

***2*-(4-chlorophenyl)-*N*-cyclohexyl-5*H*-imidazo[1,2-*b*]indazol-3-amine (4y).** Yield: 91 % (331.3 mg); Off White solid; Mp: 228-230 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 12.38 (s, 1H), 8.06 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 1H), 7.23 – 7.18 (m, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 4.81 (d, *J* = 5.3 Hz, 1H), 3.59 – 3.50 (m, 1H), 1.82 – 1.76 (m, 2H), 1.66 – 1.62 (m, 2H), 1.54 – 1.47 (m, 1H), 1.29 – 1.22 (m, 2H), 1.20 – 1.11 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 152.07, 131.81, 131.33, 129.48, 128.76, 127.01, 125.32, 123.75, 123.41, 120.00, 118.70, 115.70, 114.62, 103.37, 53.98, 33.14, 25.54, 24.26; HRMS (ESI, m/z): calcd for $C_{21}H_{21}ClN_4$ ($M+H^+$) 364.1455, found: 364.1461. Anal. Calcd: C, 69.13; H, 5.80; N, 15.36. Found: C, 68.94; H, 5.91; N, 15.63.

***N*-cyclohexyl-2-(*p*-tolyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4z).** Yield: 88 % (303.0 mg); White solid; Mp: 216-218 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 12.26 (s, 1H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.44 (d, J = 8.7 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.22 – 7.17 (m, 1H), 6.83 (t, *J* = 7.4 Hz, 1H), 4.65 (d, *J* = 5.4 Hz, 1H), 3.56 – 3.46 (m, 1H), 2.34 (s, 3H), 1.81 – 1.76 (m, 2H), 1.68 – 1.62 (m, 2H), 1.53 – 1.46 (m, 1H), 1.29 – 1.20 (m, 2H), 1.19 – 1.10 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 151.84, 136.35, 131.40, 129.27, 127.73, 125.38, 125.04, 122.61, 121.21, 118.61, 115.49, 114.50, 103.49, 54.04, 33.17, 25.57, 24.26, 20.82; HRMS (ESI, m/z): calcd for $C_{22}H_{24}N_4$ ($M+H^+$) 344.2001, found: 344.2006. Anal. Calcd: C, 76.71; H, 7.02; N, 16.27. Found: C, 76.83; H, 7.16; N, 16.29.

8-bromo-*N*-cyclohexyl-2-(3,4,5-trimethoxyphenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4aa). Yield: 92 % (458.5 mg); White solid; Mp: 238-240 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 12.37 (s, 1H), 7.85 (s, 1H), 7.44 (d, *J* = 9.1 Hz, 1H), 7.40 (s, 2H), 7.28 (dd, *J* = 9.1, 2.0 Hz, 1H), 4.83 (d, *J* = 5.6 Hz, 1H), 3.89 (s, 6H), 3.71 (s, 3H), 3.58 – 3.50 (m, 1H), 1.83 – 1.77 (m, 2H), 1.71 – 1.64 (m, 2H), 1.54 – 1.48 (m, 1H), 1.34 – 1.25 (m, 2H), 1.22 – 1.13 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 153.08, 150.18, 136.76, 130.39, 127.77, 125.66, 122.87, 121.57, 120.45, 116.74, 106.89, 104.67, 102.98, 60.16, 55.97, 53.90, 33.27, 25.57, 24.16.; HRMS (ESI, m/z): calcd for $C_{24}H_{27}BrN_4O_3$ ($M+H^+$) 498.1267, found: 498.1271. Anal. Calcd: C, 57.72; H, 5.45; N, 11.22. Found: C, 57.58; H, 5.61; N, 11.28.

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8-bromo-N-cyclohexyl-2-(2,5-dimethoxyphenyl)-5*H*-imidazo[1,2-*b*]indazol-3-amine (4ab). Yield: 90 % (422.0 mg); White solid; Mp: 233-235 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 11.96 (s, 1H), 7.95 (s, 1H), 7.50 (s, 1H), 7.42 (d, *J* = 9.1 Hz, 1H), 7.26 (dd, *J* = 9.1, 2.0 Hz, 1H), 7.11 (d, *J* = 9.1 Hz, 1H), 6.95 (dd, *J* = 9.0, 3.1 Hz, 1H), 4.55 (d, *J* = 7.5 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 3.62 – 3.51 (m, 1H), 1.80 – 1.71 (m, 2H), 1.64 – 1.55 (m, 2H), 1.50 – 1.43 (m, 1H), 1.19 – 1.09 (m, 5H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 153.21, 150.22, 149.85, 130.75, 127.72, 124.03, 120.99, 119.28, 116.44, 116.26, 114.83, 114.20, 113.22, 106.44, 104.69, 56.27, 55.51, 52.99, 33.19, 25.46, 24.18.; HRMS (ESI, m/z): calcd for $C_{23}H_{25}BrN_4O_2$ (M+H$^+$) 468.1161, found: 468.1158. Anal. Calcd: C, 58.85; H, 5.37; N, 11.94. Found: C, 58.68; H, 5.43; N, 11.98.

(**2-hydroxyphenyl)(pyrimido[1,2-*b*]indazol-3-yl)methanone (7a).** Yield: 97 % (280.3 mg); Yellow solid; Mp: 160-162 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 10.54 (s, 1H), 9.54 (s, 1H), 8.92 (s, 1H), 8.24 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.58 – 7.48 (m, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.00 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 192.32, 157.09, 152.27, 145.97, 143.30, 137.06, 134.64, 131.17, 130.70, 123.83, 123.00, 121.63, 120.76, 119.67, 117.14, 116.33, 112.53.; HRMS (ESI, m/z): calcd for $C_{17}H_{11}N_3O_2$ (M+H$^+$) 289.0851, found: 289.0854. Anal. Calcd: C, 70.58; H, 3.83; N, 14.53. Found: C, 70.43; H, 3.98; N, 14.48.

(9-bromopyrimido[1,2-*b*]indazol-3-yl)(2-hydroxyphenyl)methanone (7b). Yield: 98 % (359.6 mg); Yellow solid; Mp: 168-170 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 10.60 (s, 1H), 9.64 (s, 1H), 9.02 (s, 1H), 7.69 – 7.64 (m, 2H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.12 – 7.07 (m, 1H), 7.06 – 7.02 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 192.12, 157.27, 157.08, 155.39, 153.81, 153.77, 153.08, 147.20, 137.08, 134.85, 131.28, 131.21, 131.16, 123.63, 123.39, 119.69, 117.20, 112.63.; HRMS (ESI, m/z): calcd for $C_{17}H_{10}BrN_3O_2$ (M+H$^+$) 366.9956, found: 366.9959. Anal. Calcd: C, 55.46; H, 2.74; N, 11.41. Found C, 55.38; H, 2.91; N, 11.29.

(5-bromo-2-hydroxyphenyl)(10-fluoropyrimido[1,2-*b*]indazol-3-yl)methanone (7c). Yield: 95 % (364.2 mg); Yellow solid; Mp: 206-208 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 10.78 (s, 1H), 9.70 (s, 1H), 9.04 (s, 1H), 7.70 – 7.66 (m, 4H), 7.13 – 7.07 (m, 1H), 7.01 (d, J = 8.7 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 191.00, 156.47, 154.41, 154.38, 147.63, 142.34, 142.30, 138.02, 137.19, 133.28, 131.80, 131.74, 126.56, 123.43, 120.02, 113.18, 111.13, 105.66, 105.54, 103.60, 103.48.; HRMS (ESI, m/z): calcd for $C_{17}H_9BrFN_3O_2$ (M+H$^+$) 384.9862, found: 384.9866. Anal. Calcd: C, 52.87; H, 2.35; N, 10.88. Found: C, 52.68; H, 2.48; N, 10.94.

(5-bromo-2-hydroxyphenyl)(pyrimido[1,2-*b*]indazol-3-yl)methanone (7d). Yield: 97 % (357.2 mg); Yellow solid; Mp: 188-190 °C; ^{1}H NMR (600 MHz, DMSO- d_6) δ 10.75 (s, 1H), 9.63 (s, 1H), 8.97 (s, 1H), 8.27 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.72 – 7.64 (m, 3H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 8.7 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, DMSO- d_6) δ 190.65, 155.79, 152.38, 145.86, 143.37, 137.47, 136.48, 132.68, 130.77, 126.27, 122.52, 121.69, 120.76, 119.44, 116.35, 112.53, 110.61.; HRMS (ESI, m/z): calcd for $C_{17}H_{10}BrN_3O_2$ (M+H$^+$) 366.9956, found: 366.9958. Anal. Calcd: C, 55.46; H, 2.74; N, 11.41. Found: C, 55.06; H, 2.83; N, 11.38.

Conflicts of interest

There are no conflicts of interest to declare.

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An Approach towards the Synthesis of Novel Fused Nitrogen Tricyclic Heterocyclic Scaffolds via GBB Reaction

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