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Iodine mediated synthesis of indazolo-quinazolinones *via* a multi-component reaction

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We report an expeditious syntheses of some unreported indazolo-quninazolinone derivatives *via* an iodine mediated multi-component reaction (MCR). The MCR involved an *in-situ* generation of the 1H-indazol-3-amine derivative in ethanol followed by its reaction with the diketone and aryl aldehyde in acetonitrile. A number of compounds have been synthesized using this methodology in good yields.

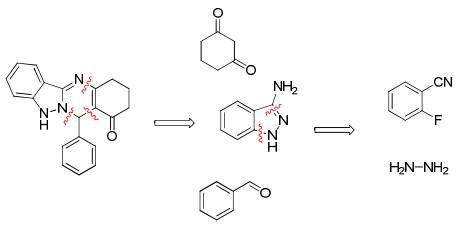
Introduction

Heterocycles has drawn a special focuses on organic chemistry due to its availability in natural products and their array of biological properties.[1] Efforts have been taken to design the synthesize and utilize the unreported heterocyclic moiety for therapeutic applications. A survey of recent literature reveals several synthesis and pharmacological properties of ring junction heterocyclic (bridge headed heterocyclic) compounds. Their interest is to provide an account of synthetize, chemical and biological properties of unreported bridge head nitrogen compounds. Contrarily, the natural abundance of nitrogen ring junction heterocycles was very less but with the available moiety many studies have been reported. Generally, quinazolinone nucleus were an important scaffold that was found in a wide range of biologically active compounds including natural product and synthetic drugs.[2-4] Camptothecin and Mappicine have been approved as a drug by FDA. Both the drugs having bridge headed nitrogen motif. It has an attracted growing interest due to their certain synthetic methodology. Further they have been provided with an importance, significance in a biological field such as anti–parasitic, antimicrobial, anticancer and antibiotic action.[5-7] Prominence in search of the atom-economy transformation with readily available reactant into the complex organic molecules,[8] were highly desirable at this juncture.[9-11] MCR represents set up of three or more reactants and convert them into higher molecular weight compound in one-pot method.[12] It has become really popular in the discovery of pharmaceutically active compounds due to their experimental simplicity, atom economy and high product yield.[13-15] From the already existing works our interest to focus on synthesizing some unreported quinazolinone – indazole fused nitrogen ring junction heterocycles. Replacement of a carbon atom in a ring junction position by heteroatoms like nitrogen, sulphur or oxygen either in five or six-membered rings leads to a wide variety of heterocycles. We have discussed on potent molecules which contains nitrogen in the ring junction position. Fascaplysin is a marine alkaloid which was originally isolated from the sponge *Fascaplysinopsis Bergquist*.[16] This red pigment exhibits a wide range of activity such as antibacterial, antifungal, antiviral, etc. Mianserin was one of the important anxiolytic or anti-depressant[17]drug. Alkaloids such as rhazinal[18] and rhazinilam[19] have potent spindle toxin by virtue of its capacity to disrupt the dynamic inter conversion of tubulin and microtubules required for the normal mitotic division of cells.[20-21] Indolizidine alkaloids such as like rhazinal and rhazinilam(-) those are derived from amphibians and ants have proved popular target for total synthesis for both structural conformation and examination of the potent bioactivity that many of these possess.[21]

In topical years, organic synthesis has received considerable attention to give the corresponding products with high selectivity in excellent yields using molecular iodine as an inexpensive reagent. The mild Lewis acidity associated with iodine enhanced its usage in organic synthesis to perform several organic transformations using stoichiometric levels to catalytic amounts. Due to advantages linked with this eco-friendly catalyst, molecular iodine has been explored as a influential reagent in organic synthesis.[22] In continuation of our earlier report in organic synthesis[23,24] we herewith reporting the molecular iodine mediated indazolo-quinazolinones synthesis.

Results and discussion

Pal. M et al., have synthesized five and six membered fused quinazolinones *via* MCR.[25] This methodology has involved with the reaction of isatoic anhydride, hydrazine and *o*-halo benzaldehyde in the presence of palladium as a catalyst. In recent literatures iodine mediated organic transformations are enriched with MCR.[26-30] Our effort is to design and synthesize some unreported nitrogen bridged head indazolo – quinazolinones under MCR condition. We have identified retro-synthetic pathway to synthesize the indazolo-quninazolinones which was outlined in **Scheme 1**. In this work, we have reported the synthesis of new series of indazolo[3,2-*b*]quinazolin-8(5*H*)-one derivatives using molecular iodine. Synthesised compounds 5(a-l) and 6(a-f) were confirmed by melting point, ^{1}H NMR, ^{13}C NMR, and HRMS analysis.

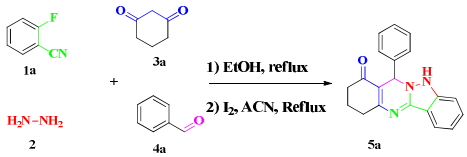


Scheme 1. The retrosynthetic route for 7-phenyl-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one from low cost and easily available reactants.

To optimize the reaction condition, we have screened with different

condition (Table 1). We have performed the reaction to synthesis 7-phenyl-7,9,10,11-tetrahydroindazolo[3,2-b]quinazolin-8(5H)-one **(5a)** in the absence of catalyst. But we end up with the negative result (Entry 1 in Table 1). We planned to utilize the catalyst to get our target compound (**5**). We have varied the catalyst such as DBU, DABCO, CAN, I_2 and CuI to get 7-phenyl-7,9,10,11-tetrahydroindazolo [3,2-b]quinazolin-8(5H)-one (Table 1). Our attempt for the synthesis of 7-phenyl-7,9,10,11-tetrahydroindazolo [3,2-b]quinazolin-8(5H)-one favour only in the presence of I_2 as a medium. We got 5% product (isolated) by using 10 mol % of molecular iodine with ethanol as a solvent. To increase the yield percentage, we have increased the iodine mol percentage from 10 to 20 mol % along with ethanol and acetonitrile (1:2) combination improves the yield up to 85%.

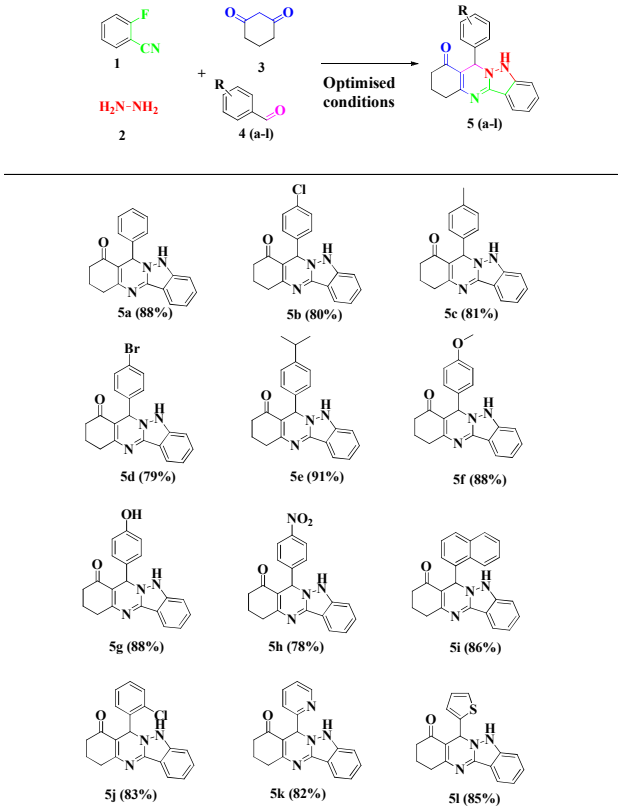
Table 1. Effect of reaction conditions on the multicomponent reaction for the synthesis of 7-phenyl-7,9,10,11-tetrahydroindazolo [3,2-b]quinazolin-8(5H)-one[a]



Entry	Solvent	Catalyst	Yield[b]
1	EtOH	-	-
2	EtOH	I_2 (10 mol%)	5%
3	EtOH	CAN (10 mol%)	-
4	EtOH	DBU	traces
6	EtOH	DABCO	-
7	EtOH	CuI (10 mol%)	-
8	EtOH/ACN	I_2 (10 mol%)	55%
9	EtOH/ACN	I_2 (20 mol%)	85%
10	EtOH/ACN	I2 (30 mol%)	45%

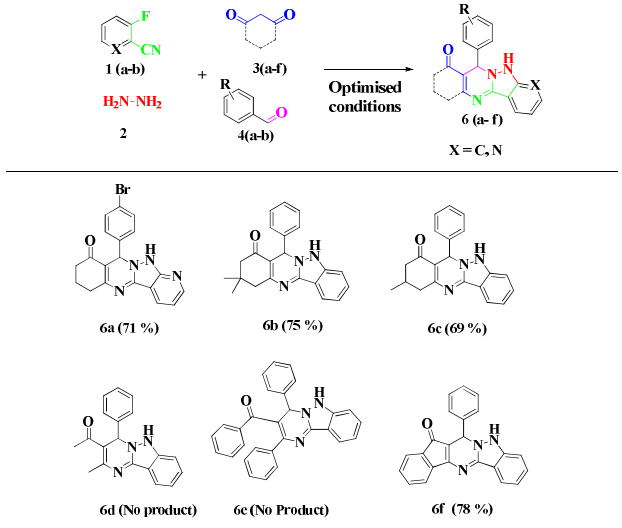
[a]Reaction conditions: 2-flurobenzonitrile (1 mmol), hydrazine hydrate (1 mmol), benzaldehyde (1 mmol) , 1,3 - cyclohexadione (1 mmol) and molecular iodine (20 mol %) in ethanol (5 mL) and acetonitrile (10 mL) at 90 ^{0}C for 4 h. Yield [b]- isolated yield

With optimized reaction condition, we have employed various aromatic aldehydes 4(a-l) to the required nitrogen ring junction compounds 5(a-l) with good to excellent yields (Scheme 2).



Scheme 2. Synthesis of indazolo[3,2-b]quinazolin-8(5H)-one derivatives

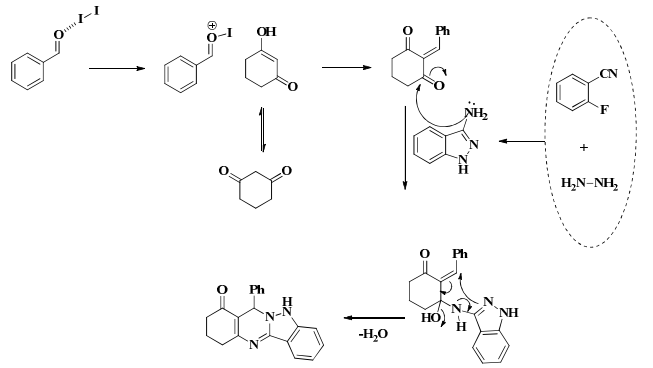
The products 5(a-l) thus obtained from the above reaction were highly selective. When we introduced wide range of functional groups like chloro, bromo, nitro, methyl, isopropyl, methoxy, and hydroxyl in the aldehyde it remains intact in the reaction condition. The electron withdrawing and electron releasing group on the phenyl motif does not provided the vast yield variations. But in the case of isopropyl derivative, we have achieved around 91% yield.



Scheme 3. Scope for various amines and dicarbonyls

The springiness of this reaction has been tested with different diketones and amines; the resultant products 6(a-f) were listed below (Scheme 3). From this above observation, we have found only cyclic

diketones which undergone such transformation and linear diketones such as acetyl acetone and dibenzoyl methane are not giving positive result.



Scheme 4. A plausible reaction mechanism for the iodine mediated MCR

This implies that cyclic diketones have been more liable to form indazolo-quninazolinones fused ring system with moderate to good yield. The proposed mechanism for the formation 7-phenyl-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one is shown in **Scheme 4**. Initially, the reaction was initiated by iodine, which reacts with aldehyde and diketone to form an adduct of diketo hydroxyl compound. On other hand the amine source was generated from 2-fluoro benzonitrile and hydrazine which react with adduct and upon loss of water molecules followed by cycloaddition to give the target product 5a**.**

Conclusion

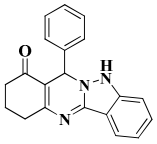
In conclusion, we have offered an efficient and easy protocol for the synthesis of indazolo-quninazolinones fused ring system through MCR using molecular iodine. Moreover, this method offers many advantages like less reaction time, noticeable yields and reactant. Some of the derivatives shown fluorescent activity, in future we planned for fluorescent and biological activities of synthesised compounds.

Experimental section

All commercially available reagents were used without any further purification and the reactions were monitored by TLC. ^{1}H and ^{13}C NMR were obtained using a Bruker Avance 400 Mz spectrometer in DMSO d_6 solvent with TMS as an internal standard. Chemical shift values (δ) were expressed in parts per million (ppm). Abbreviations are as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Melting points were measured on Elchem Microprocessor based DT apparatus using an open capillary tubes and are uncorrected. Mass spectra were obtained by high resolution mass spectrometer.

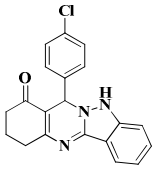
General procedure for the synthesis of 7-phenyl-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5a).
A mixture of 2-fluorobenzonitrile (1 mmol) and hydrazine (1 mmol) were mixed in 50 mL two neck round bottom flask containing 5 mL of absolute ethanol as a solvent. The mixture was refluxed for 30 min and increased the temperature to 100 ^{o}C to reduce the ethanol volume up to 90 percentages. A mixture of benzaldehyde (1 mmol), diketone (1 mmol) and iodine (20 %) in 10 ml acetonitrile was added to the reaction mixture at room temperature. Then reflux the reaction mixture and the progress of the reaction was monitored by TLC and the formed precipitate was filtered, washed with water and dried afford the product as off -white solid.

Characterization data for the compounds [5(a-i) & 6(a-f)]



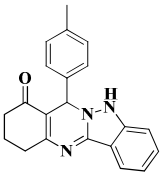
7-phenyl-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5a)

Off-White solid; Isolated yield -88 %; mp: 316-318 $^{\circ}$C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.13 (bs, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 1H), 7.26 – 7.15 (m, 6H), 6.92 (t, *J* = 8.0 Hz, 1H), 6.49 (s, 1H), 2.83 - 2.72 (m, 2H), 2.36 - 2.23 (m, 2H), 2.07 - 1.91 (m, 2H); ^{13}C NMR (100 MHz, DMSO d_6) δ 26.0, 31.5, 63.8, 110.8, 112.5, 115.9, 121.6, 124.5, 124.9, 131,8, 132.1, 132.6, 133.3, 135.2, 147.8, 152.5, 155.8, 198.1; HRMS: m/z calcd. for $C_{20}H_{17}N_3O$ 315.1372 found 315.1370.



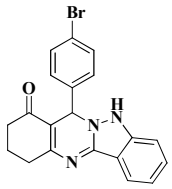
7-(4-chlorophenyl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5b)

Off-White solid; Isolated yield - 80 %; mp: 352-354 $^{\circ}$C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.20 (bs, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.36 - 7.30 (m, 3H),7.24 – 7.21 (m, 3H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.50 (s, 1H), 2.83 - 2.72 (m, 2H), 2.37 - 2.24 (m, 2H), 2.08 - 1.93 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.7, 26.3, 36.2, 58.1, 105.1, 107.2, 116.4, 119.4, 119.6, 126.7, 128.1, 128.7, 129.9, 132.0, 141.5, 147.5, 150.7, 193.0; HRMS: m/z calcd. for $C_{20}H_{16}ClN_3O$ 349.0982 found 349.0980.



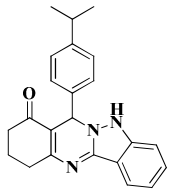
7-(p-tolyl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5c)

Off-White solid; Isolated yield - 81 %; mp: 342 – 344 $^{\circ}$C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.08 (bs, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.11 - 7.03 (m, 4H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.46 (s, 1H), 2.83 - 2.71 (m, 2H), 2.38 - 2.24 (m, 2H), 2.21 (s, 3H), 2.08 - 1.89 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.5, 20.8, 26.3, 36.3, 58.3, 105.7, 107.2, 116.4, 119.1, 119.6, 126.4, 126.7, 128.6, 129.8, 136.6, 139.8, 147.3, 150.4, 192.8; HRMS: m/z calcd. for $C_{21}H_{19}N_3O$329.1528 found 329.1520.



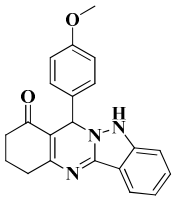
7-(4-bromophenyl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5d)

Off-White solid; Isolated yield - 79 %; mp: 358 – 360 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.19 (bs, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 8.4, 2H), 7.35 (d, *J* = 8.8, 1H), 7.21 – 7.16 (m, 3H), 6.96 - 6.92 (m, 1H), 6.48 (s, 1H), 2.83 - 2.72 (m, 2H), 2.38 - 2.23 (m, 2H), 2.08 - 1.93 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.8, 26.3, 36.2, 58.2, 105.1, 107.2, 116.4, 119.3, 119.6, 120.5, 126.6, 129.0, 129.9, 131.0, 141.9, 147.5, 150.7, 192.9; HRMS: m/z calcd. for $C_{20}H_{16}BrN_3O$ 393.0477 found 393.0470.



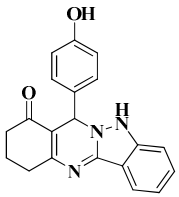
7-(4-isopropylphenyl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5e)

Off-White solid; Isolated yield - 91 %; mp: 338 - 340 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.12 (bs, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.8, 1H), 7.19 – 7.10 (m, 5H), 6.95 - 6.91 (m, 1H), 6.46 (s, 1H), 2.85 - 2.71 (m, 3H), 2.34 - 2.24 (m, 2H), 2.08 - 1.90 (m, 2H) 1.13 (d, *J* = 7.2 Hz, 6H) ;^{13}C NMR (100 MHz, DMSO d_6) δ 20.8, 23.7, 23.7, 26.3, 33.0, 36.3, 58.3, 105.6, 107.2, 116.4, 119.2, 119.6, 126.0, 126.4, 126.8, 129.8, 140.1, 147.3, 147.4, 150.5, 192.9;HRMS: m/z calcd. for $C_{23}H_{23}N_3O$ 357.1841 found 357.1840.



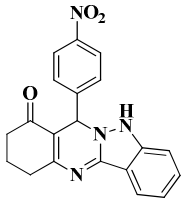
7-(4-methoxyphenyl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5f)

Off-White solid; Isolated yield - 88 %; mp: 320-322 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.08 (bs, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.34 (d, *J* = 8.8Hz, 1H), 7.19 - 7.13 (m, 3H), 6.93 (t, *J* = 6.8, 1H), 6.79 (d, *J* = 8.4Hz, 2H), 6.44 (s, 1H), 3.68 (s, 3H), 2.84 - 2.70 (m, 2H), 2.36 - 2.25 (m, 2H), 2.08 - 1.90 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.8, 26.3, 36.3, 55.0, 58.0, 105.7, 107.2, 113.4, 116.4, 119.1, 119.6, 126.4, 128.0, 129.7, 134.9, 147.3, 150.4, 158.5, 192.9; HRMS: m/z calcd. for $C_{21}H_{19}N_3O_2$ 345.1477 found 345.1470.



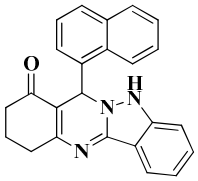
7-(4-hydroxyphenyl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5g)

Off-White solid; Isolated yield - 88 %; mp: 358 – 360 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.18 (bs, 1H), 9.36 (s, 1H), 7.35 (d, *J* = 8.8Hz, 1H), 7.19 (t, *J* = 6.8, 1H), 7.04 - 7.00 (m, 1H), 6.95 - 6.91 (m, 1H), 6.93 (t, *J* = 7.6, 1H), 6.64 - 6.55 (m, 3H), 6.40 (s, 1H), 2.82 - 2.71 (m, 2H), 2.38 - 2.26 (m, 2H), 2.06 - 1.93 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 26.0, 31.5, 41.5, 63.6, 110.9, 112.5, 118.9, 119.6, 121.7, 122.6, 124.5, 124.8, 131.8, 134.3, 135.2, 149.1, 152.6, 155.8, 162.3, 198.2; HRMS: m/z calcd. for $C_{20}H_{17}N_3O_2$ 331.1321 found 331.1320.



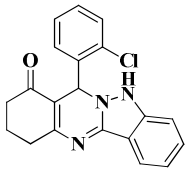
7-(4-nitrophenyl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5h)

Yellow solid; Isolated yield - 78 %; mp: 338 – 340 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.31 (bs, 1H), 8.12 (d, *J* = 8.8 Hz, 2H), 7.81 (d, *J* = 8.4Hz, 1H),7.48 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.20 (t, *J* = 6.8 Hz, 1H), 6.96 (t, *J* = 7.6, 1H), 6.63 (s, 1H), 2.84 - 2.74 (m, 2H), 2.39 - 2.25 (m, 2H), 2.08 - 1.93 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.7, 26.3, 36.2, 58.3, 104.7, 107.2, 116.5, 119.6, 119.7, 123.4, 126.8, 128.2, 130.0, 146.7, 147.6, 149.4, 151.0, 192.9; HRMS: m/z calcd. for $C_{20}H_{16}N_4O_3$ 360.1222 found 360.1220.



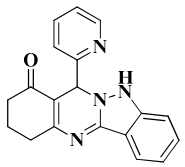
7-(naphthalen-1-yl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5i)

Yellow solid; Isolated yield - 86 %; mp: 320 – 322 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.23 (bs, 1H), 8.75 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.38 – 7.35 (m, 3H), 7.23 (d, *J* = 8.8 Hz, 1H), 7.12 (t, *J* = 6.8 Hz, 1H). 6.90 (t, *J* = 8.0, 1H), 2.94 - 2.83 (m, 2H), 2.36 - 2.20 (m, 2H), 2.19–2.00 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.9, 26.4, 36.3, 106.4, 107.2, 116.3, 119.1, 119.6, 124.2, 125.2, 125.4, 125.6, 126.1, 126.4, 128.0, 128.1, 129.5, 130.8, 133.0, 139.8, 147.1, 150.7, 192.9; HRMS: m/z calcd. for $C_{24}H_{19}N_3O$ 365.1528 found 365.1520.



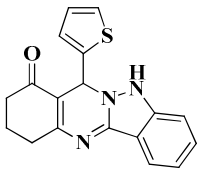
7-(2-chlorophenyl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5j)

Off-White solid; Isolated yield - 83 %; mp: 312 – 314 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.22 (bs, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.36 - 7.23 (m, 3H), 7.22 - 7.19 (m, 3H), 6.94 – 6.90 (m, 1H), 6.86 (s, 1H), 2.86 - 2.72 (m, 2H), 2.38 - 2.09 (m, 2H), 2.08 - 1.91 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.9, 26.4, 36.3, 56.6, 105.0, 106.9, 116.4, 119.2, 119.6, 126.6, 127.1, 129.0, 129.2, 129.9, 130.1, 132.2, 139.9, 147.4, 150.9, 192.8; HRMS: m/z calcd. for $C_{20}H_{16}ClN_3O$ 349.0982 found 349.0980.



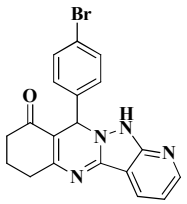
7-(pyridin-2-yl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5k)

Off-White solid; Isolated yield - 82 %; mp: 324 – 326 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.11 (bs, 1H), 8.31 (d, *J* = 4.4 Hz, 1H), 7.79 - 7.72 (m, 2H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.8 Hz, 1H), 7.20 – 7.15 (m, 2H), 6.92 (t, *J* = 8.0 Hz, 1H), 6.54 (s, 1H), 2.77 - 2.76 (m, 2H), 2.37 - 2.20 (m, 2H), 2.08 - 1.85 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.8, 26.3, 36.1, 60.2, 105.1, 107.3, 116.3, 119.1, 119.6, 122.5, 122.7, 126.5, 130.5, 136.1, 147.3, 149.1, 150.7, 159.8, 192.9 ; HRMS: m/z calcd. for $C_{19}H_{16}N_4O$ 316.1324 found 316.1320.



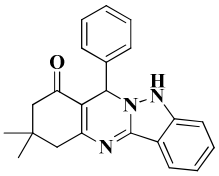
7-(thiophen-2-yl)-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (5l)

Off-White solid; Isolated yield - 85 %; mp: 318 – 320 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.24 (bs, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.34 – 7.33 (d, *J* = 4.8 Hz, 1H), 7.20 (t, *J* = 6.8 Hz, 1H), 6.95 – 6.86 (m, 3H), 6.77 (s, 1H), 2.84 - 2.76 (m, 2H), 2.38 - 2.35 (m, 2H), 2.10 - 1.98 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.8, 26.3, 36.2, 53.3, 105.1, 107.3, 116.5, 119.4, 119.6, 125.4, 125.5, 126.5, 126.6, 129.5, 145.4, 147.4, 150.9, 192.9 ; HRMS: m/z calcd. for $C_{18}H_{15}N_3OS$ 321.0936 found 321.0930.



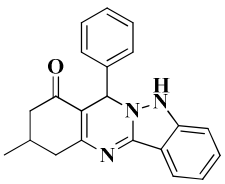
10-(4-bromophenyl)-7,8,10,12-tetrahydropyrido[2',3':3,4]pyrazolo[5,1-*b*]quinazolin-9(6*H*)-one (6a)

Off-White solid; Isolated yield - 71 %; mp: 332 – 334 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.33 (bs, 1H), 8.52 – 8.22 (m, 1H), 8.21 (d, *J* = 7.2 Hz, 1H), 7.46 (d, *J* = 8.4, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.99 - 6.96 (m, 1H), 6.49 (s, 1H), 2.81 - 2.70 (m, 2H), 2.38 - 2.25 (m, 2H), 2.08 - 1.94 (m, 2H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 20.7, 26.2, 36.2, 58.1, 99.8, 105.3, 115.6, 120.7, 129.2, 129.5, 129.7, 131.1, 141.5, 150.6, 152.1, 156.6, 193.1; HRMS: m/z calcd. for $C_{19}H_{15}BrN_4O$ 394.0429 found 394.0420.



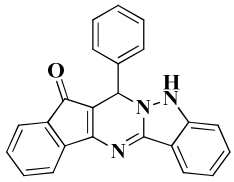
10,10-dimethyl-7-phenyl-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (6b)

Off-White solid; Isolated yield - 75 %; mp: 314-316 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.11 (bs, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 1H), 7.27 – 7.16 (m, 6H), 6.94 (t, *J* = 8.0 Hz, 1H), 6.47 (s, 1H), 2.71 - 2.60 (m, 2H), 2.98 - 2.08 (m, 2H), 1.09 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (100 MHz, DMSO d_6) δ 26.7, 28.6, 32.2, 49.8, 58.9, 104.6, 107.3, 116.4, 119.3, 126.5, 126.8, 127.4, 128.1, 130.0, 142.7, 147.4, 148.6, 192.5; HRMS: m/z calcd. for $C_{22}H_{21}N_3O$ 343.1685 found 344.1760.



10-methyl-7-phenyl-7,9,10,11-tetrahydroindazolo[3,2-*b*]quinazolin-8(5*H*)-one (6c)

Off-White solid; Isolated yield - 69 %; mp: 335-337 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.11 (bs, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.35 - 7.34 (m, 1H), 7.26 – 7.17 (m, 6H), 6.93 (t, *J* = 8.0 Hz, 1H), 6.47 (s, 1H), 2.81 - 2.76 (m, 1H), 2.66 - 2.60 (m, 1H), 2.40 – 2.26 (m, 2H), 2.15 – 2.04 (m, 1H), 1.05 (d, *J* = 4.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO d_6) δ 20.3, 28.4, 33.8, 44.2, 58.9, 105.1, 107.3, 116.4, 119.2, 119.6, 126.5, 126.8, 127.3, 128.0, 129.9, 142.6, 147.4, 149.4, 192.6; HRMS: m/z calcd. for $C_{21}H_{19}N_3O$ 329.1528 found 329.1520.



7-phenyl-5*H*-indeno[1',2':4,5]pyrimido[1,2-*b*]indazol-8(7*H*)-one (6f)

Red solid; Isolated yield - 78 %; mp: 342 – 344 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 12.31 (bs, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.40 – 7.36 (m, 1H), 7.34 – 7.23 (m, 6H), 7.06 (t, *J* = 8.0 Hz, 1H), 6.62 (s, 1H) ; ^{13}C NMR (100 MHz, DMSO d_6) δ 59.8, 102.3, 108.4, 116.9, 119.5, 119.7, 120.3, 120.7, 126.8, 127.2, 127.8, 128.3, 130.6, 131.8, 134.2, 135.4, 141.3, 147.8, 151.9, 188.1; HRMS: m/z calcd. for $C_{23}H_{15}N_3O$ 349.1215 found 349.1210.

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Notes and references

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† Electronic Supplementary Information (ESI) available.

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Graphical Abstract