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PII: S0040-4020(18)30261-8

DOI: 10.1016/j.tet.2018.03.018

Reference: TET 29358

To appear in: *Tetrahedron*

Received Date: 1 January 2018

Revised Date: 5 March 2018

Accepted Date: 8 March 2018

Please cite this article as: Arasteh Fard Z, Dilmaghani KA, Soheilizad M, Larijani B, Mahdavi M, Copper-catalyzed efficient synthesis of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones from 2-nitrobenzaldehydes, *Tetrahedron* (2018), doi: 10.1016/j.tet.2018.03.018.

Graphical Abstract

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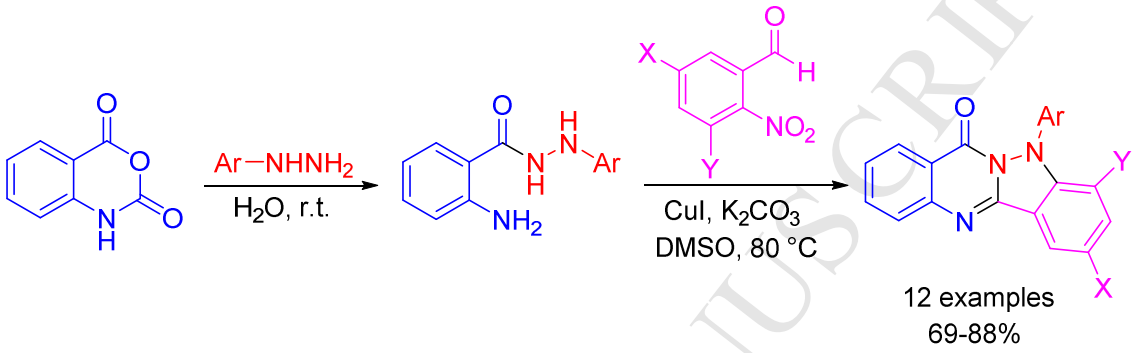

Tetrahedron
journal homepage: www.elsevier.com

Copper-catalyzed efficient synthesis of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones from 2-nitrobenzaldehydes

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Indazolo[3,2-b]quinazolinones
Copper-catalyzed
2-amino-*N'*-arylbenzohydrazide
2-nitrobenzaldehyde
intramolecular cyclization

ABSTRACT

A novel and practical copper-catalyzed approach was developed for the preparation of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones. The 2-amino-*N'*-arylbenzohydrazideis easily prepared by a reaction of isatoic anhydride with arylhydrazine. Then, through a condensation/intramolecular cyclization reaction by 2-nitrobenzaldehydes in the present of CuI, the corresponding 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones are produced in good yields.

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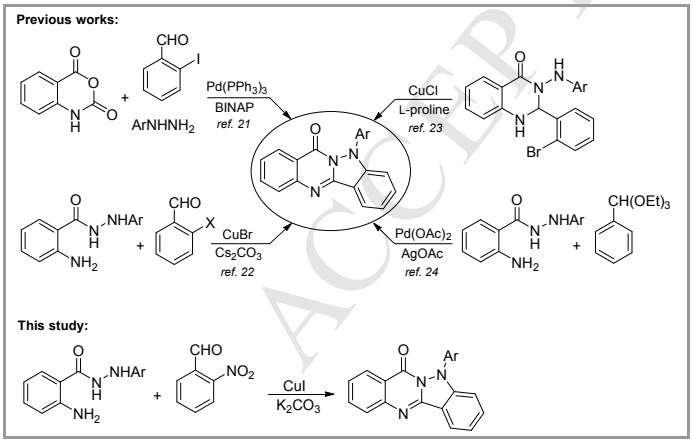
1. Introduction

Nitrogen-containing heterocyclic compounds and their analogs are pharmaceutically attractive scaffolds and widely exist in naturally occurring and synthetic biologically active molecules.[1] Among them, fused polycyclic *N*-containing heteroaromatics have received much synthetic attention because of their wide range of biological activities and their high therapeutic values.[2] For instance, *N*-fused polycycles witha quinazolinone scaffold have been shown to possess a broad range of biological activities, including anticancer,[3] anti-microbial,[4] anti-inflammatory,[5] anticonvulsant,[6] anti-ulcer,[7] anti-bacterial,[8] antidiabetic,[9] and anti-viral properties.[10] They are also an important class of alkaloids because they are widely found in the structure of a number of natural products such as luotonin A,[11] circumdatins,[12] rutaecarpine,[13] deoxyvasicinone,[14] and tryptanthrin.[15] Another example of *N*-containing biologically active heterocycles are indazole-based derivatives that have been reported to possess antidepressant,[16] anti-inflammatory,[16] HIV protease inhibitory,[17] antitumor,[18] anti-microbial,[19] and contraceptive activities.[20] The indazole core is an important pharmacophore in medicinal chemistry and has been recognized as a privileged structure in heterocyclic chemistry.

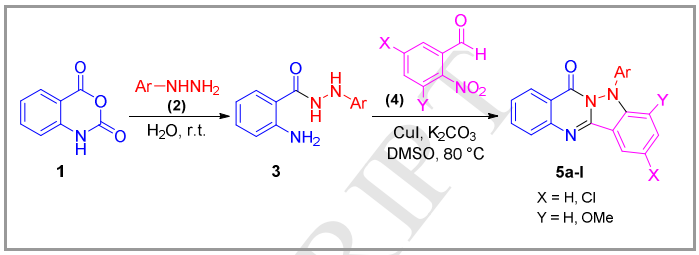
Owing to this broad range of properties of *N*-containing quinazolinone and indazole heterocycles, it is reasonable to expect that fused quinazolinone-indazole derivatives, such as indazolo[3,2-*b*]quinazolinones, have significant biological activity. To date, a few synthetic routes have been reported for the preparation of indazolo[3,2-*b*]quinazolinones, including: a one-pot cascade reaction of isatoic anhydride, hydrazines, and 2-iodo benzaldehyde catalyzed by palladium;[21] Cu-catalyzed domino Ullmann-type coupling reaction of 2-amino-*N*′-arylbenzohydrazide and 2-halobenzaldehydes;[22] intramolecularC-Nbondformationreactionof3-amino-2-(2-bromophenyl)dihydroquinazolinones by a CuCl/L-proline catalytic system;[23] and Pd-catalyzed cascade reaction of 2-amino-*N*′-arylbenzohydrazides with triethyl orthobenzoates.[24]Therefore, we wished to develop these procedures via intramolecular cyclization of 2-amino-*N*′-arylbenzohydrazide with 2-nitrobenzaldehydes catalyzed by copper(I) iodide (Scheme 1).



Scheme 1. Synthesis of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones

2. Results and discussion

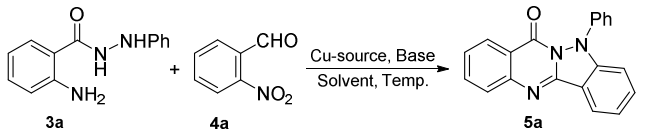
In continuation of our efforts toward the efficient synthesis of biologically active target molecules,[25] herein we would like to introduce a new approach to the preparation of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones. Thus, initially 2-amino-*N*′-arylbenzohydrazide **3** was easily prepared by the reaction of isatoic anhydride **1** and arylhydrazine **2** in aqueous media.[25] Next, heating an equimolar mixture of 2-amino-*N*′-arylbenzohydrazide **3** and 2-nitrobenzaldehydes **4** in the presence of CuI and K_2CO_3 in DMSO at 80°C for 8 hours, through a condensation and intramolecular cyclization by removal of a nitro group,[26] leads to the formation of the corresponding 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones **5a-l** in good yields (Scheme 2).



Scheme 2. Copper-catalyzed preparation of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones

To optimizethe reaction conditions, preparation of 5-phenylindazolo[3,2-b]quinazolin-7(5*H*)-one (**5a**) was investigated as a model reaction. First, we observed that heating a mixture of 2-amino-*N*′-phenylbenzohydrazide **3a** and 2-nitrobenzaldehyde **4a** in the presence of CuBr and Cs_2CO_3 in DMF as a solvent at 80°C for 8 hours lead to the desired product **5a** in 58% yield (Table 1, entry 1). Next, to evaluate the reaction medium, the effects of several solvents such as DMSO, xylene, and THF were investigated (Table 1, entries 2 to 4) and the best result was obtained in DMSO (65%, Table 1, entry 2). Then, for the choice of the best base, the model reaction was examined by various inorganic and organic bases such as K_2CO_3, K_3PO_4, DBU, and NEt_3 (Table 1, entries 5 to 8). As shown in Table 1, among various bases examined, K_2CO_3 turned out to be the best choice, while others were less effective. Next, to find the best copper source, we observed that the use of CuI as a Cu-source significantly increased the yield of **5a** (Table 1, entry 9), while the other Cu salts like CuCl, CuO, Cu_2O, and $Cu(OAc)_2$ could not enhance the yield of desired product **5a** (Table 1, entries 10 to 13). Then, to examine the effect of temperature, the model reaction in the present of CuI and K_2CO_3 in DMSO was investigated at several different temperatures (Table 1, entries 14 to 16). Finally, we observed that in the absence of Cu-catalyst, no product was formed (Table 1, entry 17). As can be seen in Table 1, the best yield of the product was obtained at 80°C (85%, Table 1, entry 9).

Table 1. Optimization of conditions for the synthesis of **5a**[a]

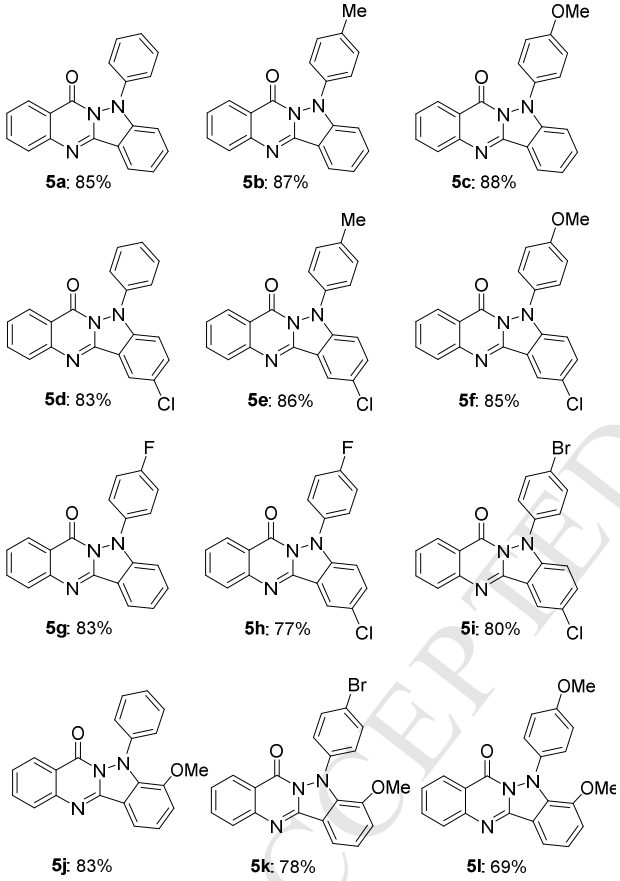


Entry	Cu source	Base	Solvent	Temp. (°C)	Yield (%)[b]
1	CuBr	$CsCO_3$	DMF	80	58
2	CuBr	$CsCO_3$	DMSO	80	65
3	CuBr	$CsCO_3$	Xylene	80	NR[c]
4	CuBr	$CsCO_3$	THF	80	32
5	CuBr	K_2CO_3	DMSO	80	68
6	CuBr	K_3PO_4	DMSO	80	48

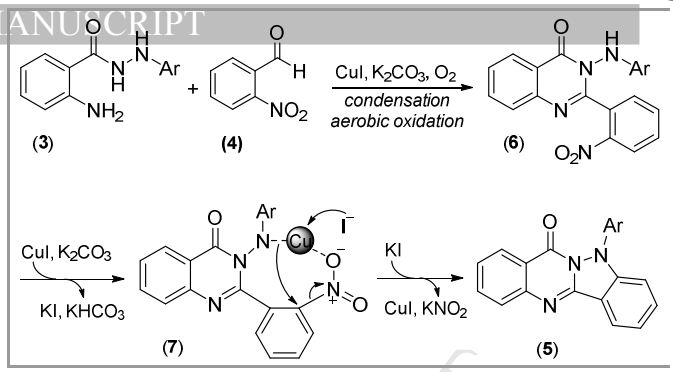
7	CuBr	DBU	DMSO	80	42
8	CuBr	NEt_3	DMSO	80	37
9	**CuI**	**K_2CO_3**	**DMSO**	**80**	**85**
10	CuCl	K_2CO_3	DMSO	80	46
11	CuO	K_2CO_3	DMSO	80	18
12	Cu_2O	K_2CO_3	DMSO	80	38
13	$Cu(OAc)_2$	K_2CO_3	DMSO	80	22
14	CuI	K_2CO_3	DMSO	120	78
15	CuI	K_2CO_3	DMSO	60	74
16	CuI	K_2CO_3	DMSO	25	15
17	–	K_2CO_3	DMSO	80	NR

[a] Reaction condition: **3a** (2 mmol), **4a** (2.1 mmol), Cu-source (0.2 mmol), Base (2 mmol), Solvent (4 mL) at reflux for 8 h. [b] Isolated yield. [c] NR= no reaction

Table 2. Substrate scope of Cu-catalyzed synthesis of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones **5a–l**



A possible reaction pathway for the Cu-catalyzed formation of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones **5** is suggested in Scheme 3. The initial condensation of the 2-amino-*N'*-arylbenzohydrazide **3** with 2-nitrobenzaldehyde **4**, followed by aerobic oxidation generate the compound **6**,[27] which undergo coordination with Cu generates intermediate **7**. Then, nucleophilic attack of iodide ion to this intermediate followed by intramolecular cyclization and libration of KNO_2, leads to the formation 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones **5** (Scheme 3).



Scheme 3. Proposed mechanism for the preparation of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones

3. Conclusion

In conclusion, we developed a new and efficient copper-catalyzed approach for the synthesis of 5-arylindazolo[3,2-*b*]quinazolin-7(5*H*)-ones through a condensation/intramolecular cyclization reaction of 2-amino-*N'*-arylbenzohydrazide with 2-nitrobenzaldehydes in the present of CuI. The simplicity of the starting materials, ligand-free metal catalysis and good yields of the products are the main advantages of this method.

4. Experimental

4.1. Material and methods

All chemicals were purchased from Merck and Fluka companies. All yields refer to isolated products. Melting points were determined in a capillary tube and have not been corrected. The progress of the reaction was followed with TLC using silica gel SILG/UV 254 and 365 plates. The IR spectra of the compounds were obtained on Nicolet FT-IR Magna 550 spectrographs (KBr disks) (Nicolet, Madison, WI, USA). ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHzon a BruckerNMR spectrometer(Rheinstetten, Germany) using tetramethylsilane (TMS) as the internal standard. Products **5e**, **5f**, **5h, 5i**, **5j**, **5k**, and **5l** are novel compounds. All products were characterized by melting point, IR, ^{1}H, and ^{13}C NMR spectroscopic data.

4.2. General procedure for the preparation of 2-amino-N'-arylbenzohydrazide (3)

A mixture of isatoic anhydride (2.0 mmol) and arylhydrazine (2.0 mmol) in H_2O (4.0 mL) was stirred for 4 hours at room temperature. After completion of the reaction as indicated by TLC, the resulting precipitate was filtered, washed with cold water, dried, and recrystallized from ethanol to produce the desired compound **3**.

4.3. General procedure for the preparation of 5-arylindazolo[3,2-b]quinazolin-7(5H)-ones (5a-i)

A mixture of 2-amino-*N'*-arylbenzohydrazide **3** (2.0 mmol), 2-nitrobenzaldehyde **4** (2.1 mmol), CuI (0.2 mmol), and K_2CO_3 (2.0 mmol) in dry DMSO (4.0 mL) was heated in a sealed vessel under air for 8 hours at 80°C. After reaction completion (checked by TLC), the reaction mixture was cooled, quenched with water (20 mL), and extracted with EtOAc (3 × 20 mL). The extract was washed with 20% NaCl solution (W/V), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by

column chromatography using petroleum ether/ethyl acetate (4:1) as the eluent to produce the pure product **5a–l**.

4.3.1. *5-phenylindazolo[3,2-b]quinazolin-7(5H)-one* (**5a**). Yield 85% (264 mg); White solid; M.p = 246–248 °C (Lit. 230–231 °C)[24]; IR (KBr, cm^{-1}): 3052, 1672, 1623, 1469, 1054; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.19 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 2H), 7.4 (t, *J* = 7.5 Hz, 2H), 7.44 (m, 3H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.80 (t, *J* = 7.5 Hz, 1H), 7.9 (d, *J* = 8.0 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.32 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 112.3, 118.8, 119.7, 123.2, 124.2, 124.5, 125.3, 126.6, 126.9, 128.5, 129.4, 133.3, 133.9, 141.8, 148.1, 148.6, 149.0, 156.3; Anal. Calcd for $C_{20}H_{13}N_3O$: C, 77.16; H, 4.21; N, 13.50. Found: C, 76.12; H, 4.17; N, 13.12.

4.3.2. *5-(p-tolyl)indazolo[3,2-b]quinazolin-7(5H)-one* (**5b**). Yield 87% (283 mg); White solid; M.p = 196–198 °C (Lit. 184–185 °C)[24]; IR (KBr, cm^{-1}): 3030, 1688, 1619, 1464, 1057; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 2.36 (s, 3H), 7.27 (d, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.52 (m, 2H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.87 (d, *J* = 6.5 Hz, 1H), 8.16 (d, *J* = 7.5 Hz,1H), 8.23 (d, *J* = 7.5 Hz,1H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 20.5, 112.5, 118.2, 119.4, 122.9, 123.7, 123.9, 124.4, 124.6, 125.1, 125.3, 125.8, 125.9, 129.8, 133.7, 133.9, 137.4, 139.2, 148.2, 148.6, 155.2; Anal. Calcd for $C_{21}H_{15}N_3O$: C, 77.52; H, 4.65; N, 12.91. Found: C, 77.47; H, 4.52; N, 12.82.

4.3.3. *5-(4-methoxyphenyl)indazolo[3,2-b]quinazolin-7(5H)-one*(**5c**). Yield 88% (301 mg); White solid; M.p = 216–218 °C (Lit. 209–210 °C)[23]; IR (KBr, cm^{-1}): 3053, 1674, 1624, 1468, 1055; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.84 (s, 3H), 6.96 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 1H), 7.3 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.79 (t, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 7.5 Hz, 1H), 8.27 (d, *J* = 7.5 Hz,1H), 8.32 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 55.5, 112.4, 114.5, 118.6, 119.8, 123.1, 124.0, 125.2, 126.6, 127.0, 133.2, 133.8, 134.4, 148.0, 148.6, 149.5, 156.4, 159.6; Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31. Found: C, 73.68; H, 4.22; N, 12.13.

4.3.4. *2-chloro-5-phenylindazolo[3,2-b]quinazolin-7(5H)-one* (**5d**). Yield 83% (287 mg); White solid; M.p = 241–243 °C (Lit. 272–273 °C)[22]; IR (KBr, cm^{-1}): 3184, 1679, 1627, 1465, 1053; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.12 (d, *J* = 8.5 Hz, 1H), 7.35 (d, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 7.0 Hz, 1H), 7.47 (m, 3H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.9 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 8.32 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ =113.6, 119.9, 120.2, 122.8, 124.5, 125.7, 126.7, 127.1, 128.8, 129.6, 130.0, 133.6, 134.1, 141.4, 147.1, 147.7, 148.4, 148.9, 155.2, 156.2; Anal. Calcd for $C_{20}H_{12}ClN_3O$: C, 69.47; H, 3.50; N, 12.15. Found: C, 69.25; H, 3.21; N, 11.94.

4.3.5. *2-chloro-5-(p-tolyl)indazolo[3,2-b]quinazolin-7(5H)-one* (**5e**). Yield 86% (309 mg); White solid; M.p = 226–228 °C; IR (KBr, cm^{-1}): 3020, 1682, 1626, 1466, 1054; ^{1}H NMR ($CDCl_3$, 500 MHz): δ =2.40 (s, 3H), 7.09 (d, *J* = 8.5 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 2H), 7.27 (d, *J* = 9.0 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.81 (t, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 8.25 (s, 1H), 8.32 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ =21.2, 113.6, 119.9, 122.7, 124.7, 125.6, 126.7, 126.7, 127.0, 127.1, 130.2, 133.5, 134.0, 138.8, 139.0, 147.6, 148.6, 156.3; Anal. Calcd for $C_{21}H_{14}ClN_3O$: C, 70.10; H, 3.92; N, 11.68. Found: C, 69.91; H, 3.58; N, 11.35.

4.3.6. *2-chloro-5-(4-methoxyphenyl)indazolo[3,2-b]quinazolin-7(5H)-one* (**5f**). Yield 85% (319 mg); White solid; M.p = 238–240 °C; IR (KBr, cm^{-1}): 3046, 1681, 1627, 1466, 1060; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.84 (s, 3H), 6.97 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 9.0 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.81 (t, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 8.25 (s, 1H), 8.32 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ =55.5, 113.7, 114.7, 117.5, 121.3, 125.0, 125.3, 125.6, 126.8, 126.9, 128.7, 129.8, 133.6, 134.0, 147.7, 156.7, 157.0, 157.3; Anal. Calcd for $C_{21}H_{14}ClN_3O_2$: C, 67.12; H, 3.76; N, 11.18. Found: C, 66.87; H, 3.48; N, 10.93.

4.3.7. *5-(4-fluorophenyl)indazolo[3,2-b]quinazolin-7(5H)-one* (**5g**). Yield 83% (273 mg); White solid; M.p = 213–215 °C (Lit. 197–198 °C)[23]; IR (KBr, cm^{-1}): 3076, 1674, 1626, 1467, 1059; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.15 (m, 3H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.43 (t, *J* = 7.0 Hz, 1H), 7.46 (t, *J* = 7.0 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 8.32 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 112.3, 116.4, 116.5, 118.9, 123.5, 124.4, 125.5, 126.6, 127.0, 127.1, 130.3, 133.4, 134.0, 143.7, 148.6, 153.6, 155.3; Anal. Calcd for $C_{20}H_{12}FN_3O$: C, 72.94; H, 3.67; N, 12.76. Found: C, 72.52; H, 3.44; N, 12.35.

4.3.8. *2-chloro-5-(4-fluorophenyl)indazolo[3,2-b]quinazolin-7(5H)-one* (**5h**). Yield 77% (281 mg); White solid; M.p = 222–224 °C; IR (KBr, cm^{-1}): 3056, 1683, 1625, 1465, 1057; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.06 (d, *J* = 8.5 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.57 (d, *J* = 8.5 Hz, 1H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 8.26 (s, 1H), 8.31 (d, *J* = 8.0 Hz, 1H);^{13}C NMR ($CDCl_3$, 125 MHz): δ = 113.6, 116.5, 116.7, 125.3, 125.4, 125.8, 125.8, 127.0, 127.1, 127.2, 130.9, 133.7, 134.3, 134.3, 136.0, 143.9, 153.1, 155.3; Anal. Calcd for $C_{20}H_{11}ClFN_3O$: C, 66.04; H, 3.05; N, 11.55. Found: C, 65.72; H, 2.87; N, 11.23.

4.3.9. *5-(4-bromophenyl)-2-chloroindazolo[3,2-b]quinazolin-7(5H)-one* (**5i**). Yield 80% (340 mg); White solid; M.p = 244–246 °C; IR (KBr, cm^{-1}): 3061, 1678, 1629, 1465, 1052; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 7.39 (d, *J* = 9.0 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.89 (t, *J* = 7.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.27 (s, 1H);^{13}C NMR ($CDCl_3$, 125 MHz): δ = 114.0, 120.8, 122.2, 124.3, 124.6, 124.7, 125.6, 126.0, 126.0, 126.4, 128.9, 132.2, 133.7, 140.4, 146.4, 147.9, 155.5; Anal. Calcd for $C_{20}H_{11}BrClN_3O$: C, 56.56; H, 2.61; N, 9.89. Found: C, 56.31; H, 2.42; N, 9.48.

4.3.10. *5-(4-methoxyphenyl)indazolo[3,2-b]quinazolin-7(5H)-one* (**5j**). Yield 83%(283 mg); White solid; M.p = 220–224 °C; IR (KBr, cm^{-1}): 3048, 1680, 1616, 1468, 1050; ^{1}H NMR (DMSO-d6, 500 MHz): δ = 3.77 (s, 3H), 6.78 (d, *J* = 7.0 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 7.0 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.53-7.77 (m, 5H-ph), 8.14 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (DMSO-d6, 125 MHz): δ = 56.4, 111.9, 115.2, 115.6, 115.7, 116.1, 117.7, 121.6, 126.1, 128.0, 128.2, 129.0, 133.5, 140.3, 146.0, 147.1, 154.3, 163.4; Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31. Found: C, 74.09; H, 4.66; N, 12.48.

4.3.11. *5-(4-bromophenyl)-4-methoxyindazolo[3,2-b]quinazolin-7(5H)-one* (**5k**). Yield 78%(328 mg); White solid; M.p = 215–219 °C; IR (KBr, cm^{-1}): 3068, 1674, 1625, 1468, 1068; ^{1}H NMR (DMSO-d6, 500 MHz): δ = 3.82 (s, 3H), 7.01 (t, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 2H), 7.52 (t, *J* = 8.0 Hz,

1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 7.5 Hz, 2H), 7.84 (d, *J* = 7.0 Hz, 1H), 7.92 (d, *J* = 7.5 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 8.30 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR (DMSO-d6, 125 MHz): δ = 56.7, 112.0, 113.8, 114.0, 115.0, 117.9, 118.9, 120.6, 126.2, 126.9, 128.0, 129.2, 131.0, 133.7, 136.7, 146.7, 154.2, 162.8; Anal. Calcd for $C_{21}H_{14}BrN_3O_2$: C, 60.02; H, 3.36; N, 10.00. Found: C, 6.28; H, 3.54; N, 10.18.

4.3.12. *4-methoxy-5-(4-methoxyphenyl)indazolo[3,2-b]quinazolin-7(5H)-one* (**5l**). Yield 69%(256 mg); White solid; M.p = 206-212 °C; IR (KBr, cm^{-1}): 3048, 1665, 1625, 1455, 1066; ^{1}H NMR (DMSO-d6, 500 MHz): δ = 3.71 (s, 3H), 3.84 (s, 3H), 6.72 (t, *J* = 7.5 Hz, 1H), 7.00 (dd, J_1= 8.5 Hz, J_2= 3.0 Hz, 2H), 7.05 (d, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.21-7.24 (m, 4H), 7.88 (d, *J* = 8.0 Hz, 1H), 8.32 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (DMSO-d6, 125 MHz): δ = 55.3, 109.9, 113.9, 114.6, 117.4, 117.8, 122.1, 127.6, 128.2, 128.8, 132.2, 133.6, 134.6, 146.7, 149.6, 149.9, 154.2, 158.5, 162.8; Anal. Calcd for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.61; N, 11.31. Found: C, 71.34; H, 4.83; N, 11.60.

Acknowledgment

This research was supported by a grant from Iran National Science Foundation (INSF).

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