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SYNTHESIS AND CHARACTERIZATION OF SOME NOVEL INDAZOLE ANALOGOUS THIAZOLIDINES FOR ANTIFUNGAL STUDY

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Abstract: A new series of 1-methyl-1*H*-indazole-3-carboxylic acid (5-benzylidene-4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazides **(6a-g)** was synthesized in good yields from 1-methyl-1*H*-indazole-3-carboxylic acid (4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazide **(5)** by operating 1-methyl-1*H*-indazole-3-carboxylic acid **(1)** as starting material and 1-methyl-1*H*-indazole-3-carboxylic acid ethyl ester **(2)**, 1-methyl-1*H*-indazole-3-carboxylic acid hydrazide **(3)**, 1-(1-methyl-1*H*-indazole-3-yl)-carbanoyl-4-phenylthiosemicarbazide **(4)** as intermediates. All the resulted compounds were characterized through spectral data and elemental analysis. Eventually, the title compounds were screened for their antifungal activity against four fungal organisms. As per the screening results, tested compounds exhibited moderate to good growth inhibition activity with a degree of variation.

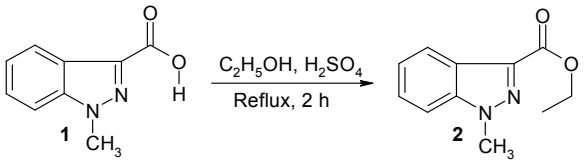
Keywords: Indazole, Thiazolidines, Antifungal study

Introduction: Indazole derivatives are important nitrogen containing nine membered bicyclic heterocyclics with several biological and pharmacological activities such as antimicrobial [I], antiproliferative [II], antiprotozoal [III] and have also been used as protein kinase inhibitors [IV] and anesthesia [V]. Thiazolidine ring system derives special important from the fact that it plays important role in medicinal chemistry with wide range biological activities like antifungal [VI], antiproliferative [VII], anti-inflammatory [VIII], antimalarial [IX], herbicidal [X], and antiviral [XI].

Results and discussion: Inspired by the activity nature of both indazole and thiazolidine, we turned our attention to the synthesis and investigation of their counterparts. In the present study, we reported the synthesis of a novel series of 1-methyl-1*H*-indazole-3-carboxylic acid (5-benzylidene-4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazides **(6a-g)** and their antifungal evaluation is described. The general synthetic route leading to the target compounds is illustrated in Schemes 1-5.

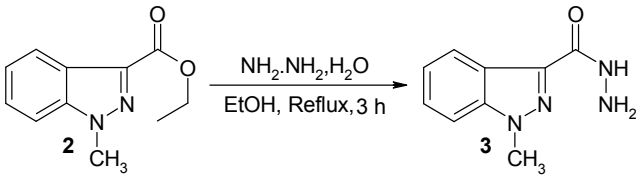
The initial intermediate as per reported in the scheme 1, 1-methyl-1*H*-indazole-3-carboxylic acid ethyl ester **(2)** through esterification was obtained by treating the starting material, 1-

methyl-1*H*-indazole-3-carboxylic acid **(1)** with ethyl alcohol in presence of catalytic amount of sulphuric acid under reflux on water bath with constant stirring for 2 h. From the spectral and elemental analysis data, compound **2** has been in conformity with structure envisaged. The new CH_3-CH_2 and C-O linkages in the IR spectrum were identified at expected absorption bands. Different from compound **1**, the ^{1}H-NMR spectrum of compound **2** exhibited additional signals due to CH_3-CH_2 moiety as triplet and quartet with constant coupling constant (J) at δ- chemical shifts 3.36 ppm and δ 2.48 ppm. The mass spectrum of the compound contains the peak corresponding to its molecular weight 204.



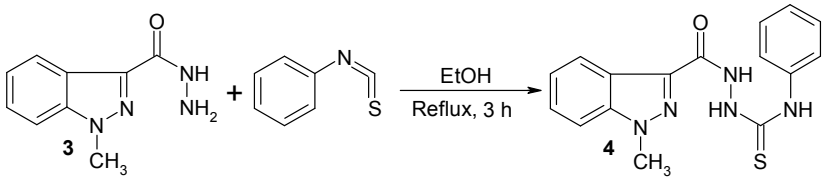
Scheme 1

Then, compound **2** was treated with hydrazine hydrate in ethanol at reflux temperature with uniform stirring on water bath for 3 h to offer the next intermediate, 1-methyl-1*H*-indazole-3-carboxylic acid hydrazide **(3)** in good yield (Scheme 2). The evidence for the formation of compound **3** can be obtained by the IR, NMR, mass spectroscopic methods and elemental analysis. IR spectrum of compound **3** shows a few broad bands between 3325−3218 cm^{-1} confirming the presence of NH_2-NH groups. Its ^{1}H NMR spectrum shows a broad singlet at δ 4.45 ppm due to NH_2 exchangeable proton and the additional NH proton resonated as singlet at about δ 7.70 ppm. In the MS spectrum, the molecular ion peak at m/z 190 indicated the formation of compounds **3**.



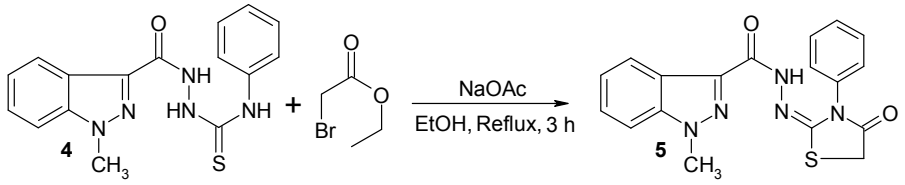
Scheme 2

Moreover, the third intermediate, 1-(1-methyl-1*H*-indazole-3-yl)-carbanoyl-4-phenylthiosemicarbazide **(4)** was obtained in good yield by treating compound **3** with phenyl isothiocyanate under reflux for 3 h with steady stirring on water bath (Scheme 3). The structure of compound **4** was confirmed on the basis of IR, NMR, and mass spectroscopic data and elemental analysis. The IR spectrum displayed broad stretching bands between 3374-3318 cm^{-1} due to N-H absorptions and C=S stretching was observed at 1210 cm^{-1} which was absent in precursor **3**. In the ^{1}H NMR spectrum, a signal in the region δ 7.65-7.37 ppm as multiplet for nine protons is assignable to two aromatic rings. Moreover, the additional signal due to the N-H group was observed at δ 8.71 ppm (D_2O not exchangeable), while the NH_2 group is converted into NH. In addition, the relatively stable molecular ion peak is observed at m/z 325 in the corresponding mass spectrum confirmed this conversion.



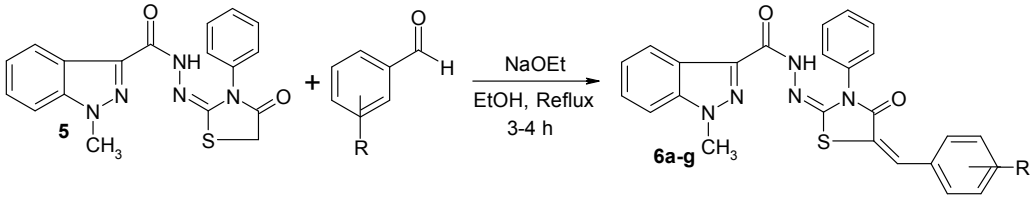
Scheme 3

The final intermediate, 1-methyl-1*H*-indazole-3-carboxylic acid (4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazide **(5)** was obtained in sound yield from the cyclization between compound **4** and ethyl bromoacetate with sodium acetate in ethanol at reflux temperature on water bath with stable stirring for 3 h (Scheme 4). The structure of this compound was established by elemental analysis and on the basis of their mass, infrared and nuclear magnetic resonance spectra. In the IR spectrum, an additional band at 1638 cm^{-1} was obtained due to another C=O stretching in place of 1210 cm^{-1} of C=S stretching. In the ^1H NMR spectrum, the signals for two NH groups were disappeared and a new signal at δ 4.25 pm as singlet for two protons corresponding to the CH_2 group which is part of five membered ring as expected for the formation of compound **5**. The mass spectrum showed a molecular ion peak in agreement with its molecular formula.



Scheme 4

Furthermore, the title compounds, 1-methyl-1*H*-indazole-3-carboxylic acid (5-benzylidene-4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazides **(6a-g)**, have been achieved at satisfactory yields through condensation between compound **5** and various aromatic aldehydes with sodium ethoxide in reflux ethanol with invariable stirring in water bath for 3-4 h (Scheme 5). The spectral data of this series of compounds was in accordance with the proposed structures. In the ^1H NMR spectrum, a new singlet signal was found at δ 4.62 ppm of CH group which is generated from the condensation in addition to the remaining signals. The molecular ion peak is observed in case of **6a** at m/z 543 corresponding to its molecular weight. The rest of compounds of this class have been emerged with expected chemical structures.



Scheme 5

6 (a) = H, (b) = 2-Cl, (c) = 4-Cl, (d) = 2-Br, (e) = 4-Br, (f) = 2-NO_2, (g) = 4-NO_2

Antifungal Activity

Finally, the title compounds, 1-methyl-1*H*-indazole-3-carboxylic acid (5-benzylidene-4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazides **(6a-g)** have been used to find their anti fungal ability in form of minimum inhibitory concentration MIC (µg/ml) towards four fungal organisms such as *Candida albicans, Aspergillus fumigatus, Trichophyton rubrum* and *Trichophyton mentagrophytes* through broth dilution method [XII] by using dimethyl sulfoxide (DMSO) as solvent and Amphotericin B as standard drug. As per the screening results reported in the Figure 1, compound **6a** against *T. Rubrum*, **6b** towards except *C. albicans*, **6g** averse to *A. fumigates* and *T. Rubrum* performed highest anti fungal activity at MIC 7.0 µg/ml. On the other hand, product **6a** opposed to *C. Albicans*, **6c** hostile to excluding *A. fumigatus*, **6d** in the direction of all fungal organisms, **6e** so as to near *C. albicans* and *A. fumigates* and product **6f** towards except *T. Rubrum* exhibited minimum

fungal activity at the MIC 24.5 µg/ml. Remaining screening study was found at moderate activity against the fungal organisms employed at MIC 14.0 µg/ml and 10.5 µg/ml as compared with standard.

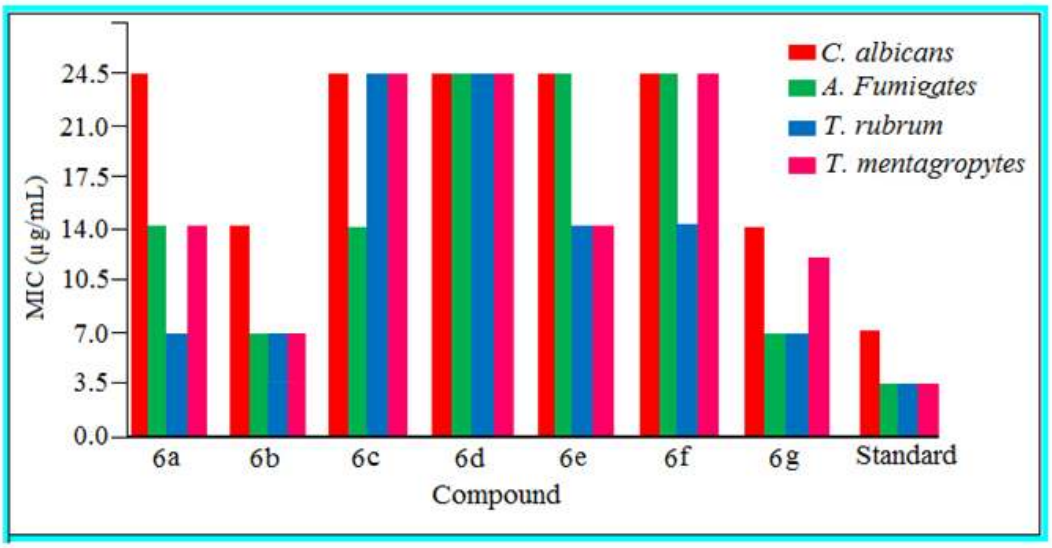


Figure 1: Antifungal activity of compounds 6a-g

Experimental section

All chemicals and reagents were obtained from commercial sources and were used as supplied, without further purification. Melting points were determined with a Fisher–Johns melting point meter in the open glass capillary method and are uncorrected. The reaction progress and purity of the synthesized compounds were monitored by analytical thin layer chromatography (TLC) using Merck precoated Silica Gel $60F_{254}$ sheets. IR spectra were recorded on a Perkin-Elmer BX serried FTIR 5000 spectrometer using KBr pellet. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at room temperature on a Varian spectrometer at 300 MHz and 100 MHz operating frequency using tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on a VG-Micromass 7070H spectrometer operating at 70 eV.

1-methyl-1H-indazole-3-carboxylic acid ethyl ester (2) To the solution of 1-methyl-1*H*-indazole-3-carboxylic acid **(1)** (0.01 mol) in ethanol (20 ml) was added conc. H_2SO_4 (1 ml). The resulted solution was refluxed for 2 h with constant stirring on water bath. After completion of the reaction (monitored by the TLC), the generated solid was filtered, washed with cold-water, dried and recrystallized from ethanol to offer pure 1-methyl-1*H*-indazole-3-carboxylic acid ethyl ester **(2)**. Yield: 68%; mp: 123-125 °C; IR (KBr): 3020 (C-H, Ar), 2966 (C-H, CH_3), 1740 (C=O), 1572 (C=C, Ar), 1445 (C=N), 1135 (C-O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.49-7.36 (m, 4H, Ar-H), 3.36 (q, 2H, J = 5.2 Hz, CH_2), 3.21 (s, 3H, N-CH_3), 2.48 (t, 3H, J = 5.2 Hz, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 146.1, 135.6, 132.0, 130.8, 127.8, 125.7, 124.2, 55.7, 47.6, 28.1. MS: *m/z* 204 (M^+); Elemental analysis: Calculated for $C_{11}H_{12}N_2O_2$: C-64.69, H-5.92, N-13.72, O-15.67. Found: C-63.87, H-5.91, N-13.69, O-15.59.

1-methyl-1H-indazole-3-carboxylic acid hydrazide (3) A solution of compound **2** (0.01 mol) and hydrazine hydrate (15 ml) in ethanol (20 ml) was refluxed on water bath with steady

stirring for 3 h. After realization of the reaction (examined by the TLC), the reaction mixture was cooled, poured in ice-cold water (20 ml) thus the resulted solid was filtered, dried and recrystallized from ethanol to offer 1-methyl-1*H*-indazole-3-carboxylic acid hydrazide **(3)** in pure form. Yield: 70%; mp: 130-132 °C; IR (KBr): 3325 (N-H, NH_2), 3218 (N-H, NH), 3032 (C-H, Ar), 2971 (C-H, CH_3), 1662 (C=O), 1582 (C=C, Ar), 1449 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.70 (s, 1H, NH), 7.46-7.38 (m, 4H, Ar-H), 4.45 (s, 2H, NH_2), 3.24 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.8, 143.8, 133.8, 131.2, 129.7, 126.3, 124.5, 123.7, 48.6. MS: *m/z* 190 (M^+); Elemental analysis: Calculated for $C_9H_{10}N_4O$: C-56.83, H-5.30, N-29.45, O-8.41. Found: C-55.98, H-5.29, N-29.21, O-8.40.

1-(1-methyl-1H-indazole-3-yl)-carbanoyl-4-phenylthiosemicarbazide (4) A mixture of compound **3** (0.01 mol) and phenyl isothiocyanate (0.01 mol) in ethanol (15 ml) was heated under reflux with uniform stirring on water bath for 3 h. After achievement of the reaction (scanned by the TLC), the residual mass was poured over crushed ice, filtered, washed with water, dried and recrystallized from ethanol to get the pure 1-(1-methyl-1*H*-indazole-3-yl)-carbanoyl-4-phenylthiosemicarbazide **(4)**. Yield: 73%; mp: 136-138 °C; IR (KBr): 3374 (N-H), 3318 (N-H), 3028 (C-H, Ar), 2975 (C-H, CH_3), 1668 (C=O), 1575 (C=C, Ar), 1439 (C=N), 1210 (C=S) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 8.71 (s, 1H, NH), 8.48 (s, 1H, NH), 7.68 (s, 1H, NH), 7.65-7.37 (m, 9H, Ar-H), 3.28 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.3, 152.3, 146.7, 140.2, 136.5, 135.2, 132.7, 130.7, 128.6, 125.3, 123.1, 122.9, 120.7, 46.2. MS: *m/z* 325 (M^+); Elemental analysis: Calculated for $C_{16}H_{15}N_5OS$: C-59.06, H-4.65, N-21.52, O-4.92, S-9.85. Found: C-58.12, H-4.64, N-21.41, O-4.91, S-9.84.

1-methyl-1H-indazole-3-carboxylic acid (4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazide (5) To a solution of compound **4** (0.01 mol) and sodium acetate (0.05 mol) in ethanol (15 ml) was added ethyl bromoacetate (0.01 mol). Thus the developed mixture was heated under reflux for 6 h on water bath with steady stirring. After fulfilment of the reaction (scrutinized by the TLC), the mixture was cooled, filtered and recrystallized from ethanol to give pure 1-methyl-1*H*-indazole-3-carboxylic acid (4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazide **(5)**. Yield: 75%; mp: 118-120 °C; IR (KBr): 3336 (N-H), 3035 (C-H, Ar), 2970 (C-H, CH_3), 1658 (C=O), 1638 (C=O), 1582 (C=C, Ar), 1452 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.72 (s, 1H, NH), 7.71-7.35 (m, 9H, Ar-H), 4.25 (s, 2H, CH_2), 3.32 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 161.8, 145.3, 143.2, 138.2, 135.7, 133.2, 131.2, 130.2, 127.2, 124.6, 122.0, 120.3, 116.3, 46.2, 39.2. MS: *m/z* 365 (M^+); Elemental analysis: Calculated for $C_{18}H_{15}N_5OS$: C-59.16, H-4.14, N-19.17, O-8.76, S-8.78. Found: C-58.21, H-4.13, N-19.10, O-8.75, S-8.77.

1-Methyl-1H-indazole-3-carboxylic acid (5-benzylidene-4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazide (6a) A mixture of compound **5** (0.01 mol) and benzaldehyde (0.01 mol) in presence of sodium ethoxide (0.02 mol) in absolute ethanol (20 ml) was heated at reflux temperature with static stirring on water bath for 3 h. After execution of the reaction (inspected by the TLC), the mixture was cooled to room temperature, poured into ice-cold water, neutralized with HCl solution and obtained crude was filtered, dried and recrystallized from ethanol to afford pure 1-methyl-1*H*-indazole-3-carboxylic acid (5-benzylidene-4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazide **(6a)**. The rest of compounds **(6b-g)** of this series have been prepared by following the similar procedure. Yield: 72%; mp: 136-138 °C; IR (KBr): 3354 (N-H), 3032 (C-H, Ar), 2938 (C-H, CH_3), 1662 (C=O), 1562 (C=C, Ar), 1442 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.78 (s, 1H, NH), 7.75-7.30 (m, 14H, Ar-H), 4.62 (s, 1H, CH), 3.36 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.7, 163.2,

148.1, 145.6, 141.8, 139.7, 137.2, 135.3, 133.7, 132.1, 130.8, 129.6, 127.6, 126.2, 125.3, 124.3, 122.8, 120.5, 119.2, 116.3, 48.2. MS: *m/z* 543 (M^+); Elemental analysis: Calculated for $C_{25}H_{19}N_5O_2S$: C-66.21, H-4.22, N-15.44, O-7.06, S-7.07. Found: C-65.32, H-4.21, N-15.40, O-7.05, S-7.06. ***1-Methyl-1H-indazole-3-carboxylic acid [(5-(2-chloro-benzylidene)-4-oxo-3-phenyl-thiazolidin-2-ylidene]-hydrazide (6b):*** Yield: 77%; mp: 145-147 °C; IR (KBr): 3358 (N-H), 3038 (C-H, Ar), 2940 (C-H, CH_3), 1656 (C=O), 1553 (C=C, Ar), 1437 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.81 (s, 1H, NH), 7.71-7.33 (m, 13H, Ar-H), 4.65 (s, 1H, CH), 3.42 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.3, 164.3, 149.7, 144.3, 142.8, 140.7, 139.3, 137.2, 135.8 134.7, 132.3, 131.8, 130.7, 129.3, 129.3, 127.8, 126.2, 125.7, 123.7, 122.1, 121.2, 119.7, 49.1. MS: *m/z* 487 (M^+); Elemental analysis: Calculated for $C_{25}H_{18}ClN_5O_2S$: C-61.54, H-3.72, Cl-7.27, N-14.35, O-6.56, S-6.57. Found: C-60.47, H-3.71, Cl-7.26, N-14.33, O-6.55, S-6.56. ***1-Methyl-1H-indazole-3-carboxylic acid [(5-(4-chloro-benzylidene)-4-oxo-3-phenyl-thiazolidin-2-ylidene]-hydrazide (6c):*** Yield: 71%; mp: 112-114 °C; IR (KBr): 3342 (N-H), 3036 (C-H, Ar), 2948 (C-H, CH_3), 1666 (C=O), 1560 (C=C, Ar), 1445 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.83 (s, 1H, NH), 7.69-7.29 (m, 9H, Ar-H), 7.65 (d, 2H, J = 7.5 Hz, Ar-H), 7.42 (d, 2H, J = 7.5 Hz, Ar-H), 4.60 (s, 1H, CH), 3.38 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.3, 162.7, 147.2, 144.7, 140.3, 138.1, 136.2, 134.7, 132.3, 131.2, 129.7, 128.3, 126.7, 125.1, 124.7, 123.2, 121.0, 119.7, 117.2, 114.7, 46.7. MS: *m/z* 487 (M^+); Elemental analysis: Calculated for $C_{25}H_{18}ClN_5O_2S$: C-61.54, H-3.72, Cl-7.27, N-14.35, O-6.56, S-6.57. Found: C-60.47, H-3.71, Cl-7.26, N-14.33, O-6.55, S-6.56. ***1-Methyl-1H-indazole-3-carboxylic acid [(5-(2-bromo-benzylidene)-4-oxo-3-phenyl-thiazolidin-2-ylidene]-hydrazide (6d):*** Yield: 75%; mp: 135-137 °C; IR (KBr): 3358 (N-H), 3042 (C-H, Ar), 2940 (C-H, CH_3), 1661 (C=O), 1558 (C=C, Ar), 1436 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.85 (s, 1H, NH), 7.77-7.37 (m, 13H, Ar-H), 4.69 (s, 1H, CH), 3.44 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.3, 163.2, 148.7, 143.2, 141.5, 139.2, 138.1, 136.8, 134.7, 133.2, 131.2, 130.5, 129.7, 128.3, 127.5, 126.5, 125.6, 124.7, 122.6, 121.2, 120.3, 118.6, 48.6. MS: *m/z* 532 (M^+); Elemental analysis: Calculated for $C_{25}H_{18}BrN_5O_2S$: C-56.40, H-3.41, Br-15.01, N-13.15, O-6.01, S-6.02. Found: C-55.57, H-3.40, Br-14.91, N-13.06, O-6.00, S-6.01. ***1-Methyl-1H-indazole-3-carboxylic acid [(5-(4-brom-benzylidene)-4-oxo-3-phenyl-thiazolidin-2-ylidene]-hydrazide (6e):*** Yield: 74%; mp: 121-123 °C; IR (KBr): 3360 (N-H), 3052 (C-H, Ar), 2944 (C-H, CH_3), 1670 (C=O), 1580 (C=C, Ar), 1439 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.78 (s, 1H, NH), 7.73-7.31 (m, 9H, Ar-H), 7.67 (d, 2H, J = 7.3 Hz, Ar-H), 7.40 (d, 2H, J = 7.3 Hz, Ar-H), 4.63 (s, 1H, CH), 3.41 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 161.7, 145.8, 143.2, 141.0 139.6, 135.3, 133.2, 131.7, 130.3, 128.7, 127.2, 125.3, 124.7, 123.2, 122.0, 120.2, 117.5, 115.3, 113.2, 44.7. MS: *m/z* 532 (M^+); Elemental analysis: Calculated for $C_{25}H_{18}BrN_5O_2S$: C-56.40, H-3.41, Br-15.01, N-13.15, O-6.01, S-6.02. Found: C-55.57, H-3.40, Br-14.91, N-13.06, O-6.00, S-6.01. ***1-Methyl-1H-indazole-3-carboxylic acid [(5-(2-nitro-benzylidene)-4-oxo-3-phenyl-thiazolidin-2-ylidene]-hydrazide (6f):*** Yield: 75%; mp: 133-135 °C; IR (KBr): 3367 (N-H), 3050 (C-H, Ar), 2952 (C-H, CH_3), 1664 (C=O), 1582 (C=C, Ar), 1444 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.88 (s, 1H, NH), 7.80-7.43 (m, 13H, Ar-H), 4.71 (s, 1H, CH), 3.46 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.6, 164.2, 149.7, 144.7, 142.3, 140.7, 137.5, 134.1, 133.7, 132.0, 130.2, 129.5, 128.1, 127.6, 126.5, 125.1, 124.8, 123.6, 121.7, 120.6, 119.8, 117.5, 47.2. MS: *m/z* 498 (M^+); Elemental analysis: Calculated for $C_{25}H_{18}N_6O_4S$: C-60.23, H-3.64, N-16.86, O-12.84, S-6.43. Found: C-59.56, H-3.70, Cl-7.24, N-14.29, O-6.54, S-6.55. ***1-Methyl-1H-indazole-3-carboxylic acid [(5-(4-nitro-benzylidene)-4-oxo-3-phenyl-thiazolidin-2-ylidene]-hydrazide (6g):*** Yield: 76%; mp: 129-131 °C; IR (KBr): 3365 (N-H), 3053 (C-H, Ar), 2945 (C-H, CH_3), 1668 (C=O), 1575 (C=C, Ar), 1439 (C=N) cm^{-1}; ^1H NMR (300 MHz, DMSO-

d_6): δ 7.75 (s, 1H, NH), 7.70-7.33 (m, 9H, Ar-H), 7.70 (d, 2H, J = 7.2 Hz, Ar-H), 7.43 (d, 2H, J = 7.2 Hz, Ar-H), 4.66 (s, 1H, CH), 3.45 (s, 3H, N-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.5, 160.5, 146.3, 144.2, 142.7 140.8, 136.5, 134.7, 132.8, 131.2, 129.6, 128.7, 126.2, 125.3, 124.8, 123.9, 121.7, 118.5, 116.2, 115.1, 47.8. MS: *m/z* 498 (M^+); Elemental analysis: Calculated for $C_{25}H_{18}N_6O_4S$: C-60.23, H-3.64, N-16.86, O-12.84, S-6.43. Found: C-59.56, H-3.70, Cl-7.24, N-14.29, O-6.54, S-6.55.

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