

Research Article

A microwave assisted, facile synthesis and antimicrobial, antitubercular evaluation of 4-(2-aryl-4-oxo-1,3-thiazolidine)-5-mercapto-3-(5-nitroindazolyl)-1,2,4-triazoles

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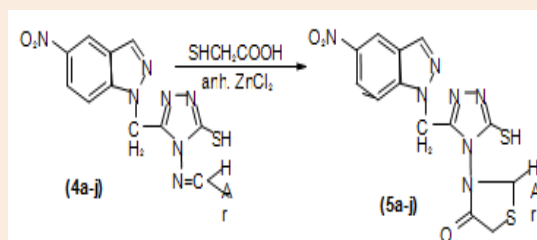
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Abstract

As a part of our research to develop novel antimicrobial and antitubercular agents, a series of 4-(2-aryl-4-oxo-1,3-thiazolidine)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (**5a-j**) have been synthesized by conventional as well as microwave method. The structures of these compounds were confirmed by IR, ¹H NMR, ¹³C NMR, FAB-mass spectra and also by microanalytical data. These compounds were tested for antibacterial activity against gram positive and gram negative organisms, antifungal activity against pathogenic strains of fungi and antitubercular activity against *Mycobacterium tuberculosis* H37Rv strain.

Keywords: 5-nitroindazole, thiazolidinone, conventional and microwave irradiation, antimicrobial and antitubercular agents

Among them tested, many compounds showed good to excellent antimicrobial and antitubercular activity.



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Introduction

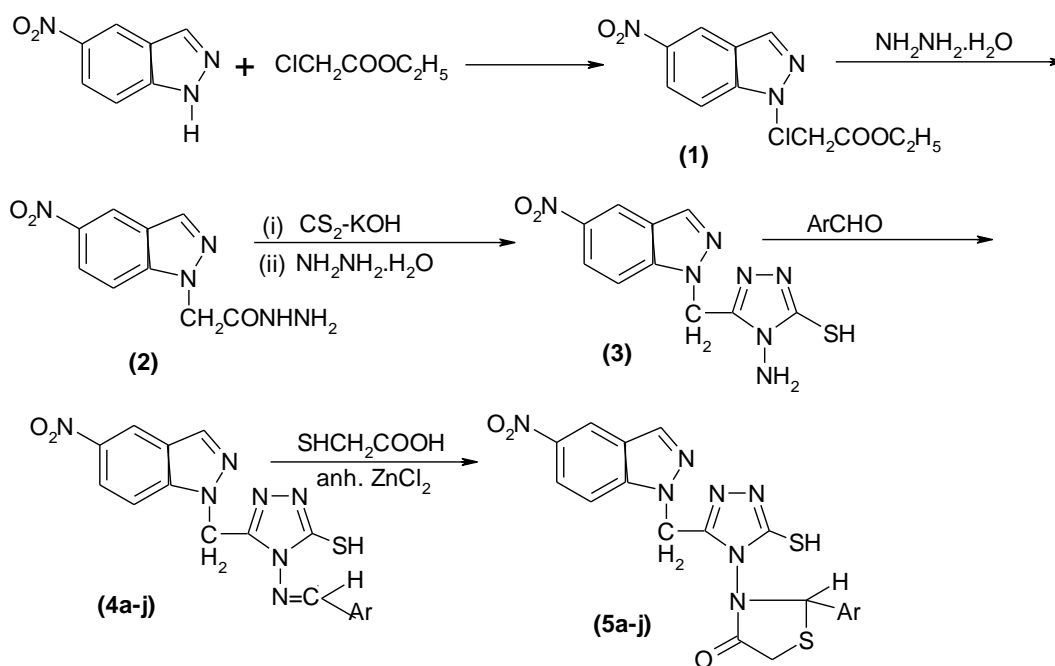
Tuberculosis (TB) is a common and often deadly infectious disease caused by mycobacteria usually *Mycobacterium tuberculosis* in humans.¹ Tuberculosis usually attacks the lungs but can also affect other parts of the body. It is spread through air, when people who have the disease cough, sneeze or spit. Unfortunately, nowadays TB is becoming again a world-wide problem, declared in 1993 by the World Health Organization (WHO), a global health emergency. The resurgence of TB became a serious world-wide problem during the period 1985-1992, particularly in people infected with the HIV virus. However, there are also other problems that contribute to the increasing incidence of TB nowadays, such as immigration, war, famine, the lack of new drugs, and multi-drug-resistant tuberculosis (MDR TB) that arise from inconsistent or partial treatment.²⁻⁸ At present, according to statistics, TB kills four people every minute somewhere in the world and accounts about two million deaths per year. It is estimated that one-third of the world's population is currently infected with the TB Bacillus and 30 million people will die in the next 10 year. In this context, there is an urgent need for new drugs to fight against this disease.

5-nitroindazole and its derivatives have been found to possess wide spectrum of activities like antiprotozoal⁹, antimalarial¹⁰, cytotoxic¹¹, antineoplastic¹², antichagasic and trypanocidal.¹³ Thiazolidin-4-ones are an important group of heterocyclic compounds, having valuable biological activities in the areas of medicine. Recently antimicrobial and antimycobacterial activities.¹⁴⁻¹⁶ of this framework containing compounds were explored well whereas their 2,3-disubstituted analogues have proved to be predominantly effective non-nucleoside HIV reverse transcriptase inhibitors.¹⁷ Microwave reactions under solvent free conditions are attractive offering reduced pollution, low cost and offer high yields together with simplicity in processing and handling.^{18,19} The salient features of microwave approach are shorter reaction times, simple reaction conditions and enhancements in yields.

The biological significance of these class of heterocycles and important features of microwave assisted synthesis impelled us to synthesize some new 4-(2-aryl-4-oxo-1, 3-thiazolidine)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (**5a-j**) have been synthesized by conventional as well as microwave methods. The structures of all the synthesized compounds were confirmed by IR, ^1H NMR, ^{13}C NMR, FAB-mass spectra and also by microanalytical data. The compounds **5a-j** have been screened for their antibacterial, antifungal and antitubercular activity.

Results and Discussion

Chemistry



Compd. 4,5	Ar	Compd. 4,5	Ar
a	C_6H_5	f	2- BrC_6H_4
b	2- ClC_6H_4	g	3- BrC_6H_4
c	4- ClC_6H_4	h	2- $\text{OCH}_3\text{C}_6\text{H}_4$
d	2- $\text{NO}_2\text{C}_6\text{H}_4$	i	4- $\text{OCH}_3\text{C}_6\text{H}_4$
e	3- $\text{NO}_2\text{C}_6\text{H}_4$	j	4- $\text{CH}_3\text{C}_6\text{H}_4$

Scheme 1

5-Nitroindazole on reaction with ethyl chloroacetate yielded N-(ethyl ethanoate)-5-nitroindazole (**1**). The formation of compound **(1)** was confirmed by the appearance of a signal at δ 1.25 and δ 4.25 ppm due to CH_3 and CH_2 respectively in $-\text{COOCH}_2\text{CH}_3$ ($J = 7$ Hz) in the ^1H NMR spectra and IR spectral band due to 1730 cm^{-1} ($>\text{C}=\text{O}$ of ester) also confirmed the formation of compound **(1)**. The compound **(1)** on amination with hydrazine hydrate yielded N-(acetyl hydrazino)-5-nitroindazole (**2**). In the ^1H NMR spectra of **(2)** a peak at δ 8.20 ppm was observed due to CONH- and a peak at δ 4.45 ppm was due to $-\text{NH}_2$. Furthermore, in the IR spectra, the bands at 1678 cm^{-1} ($>\text{C}=\text{O}$ of amide) and $3252, 3378\text{ cm}^{-1}$ ($-\text{NHNH}_2$) also confirmed the formation of compound **(2)**. The compound **2** on reaction with carbon

disulphide in the presence of ethanolic potassium hydroxide followed by treatment with hydrazine hydrate afforded 4-amino-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazole compound **3**. In the IR spectrum of the compound **3**, the bands at 3204, 3305 cm^{-1} for NH_2 and 2581 cm^{-1} for $-\text{SH}$ were observed. In the ^1H NMR spectrum, the peak at 5.51 ppm was due to NH_2 . Furthermore in the ^{13}C NMR spectrum a peak at δ 152.70 ppm due to (1,2,4-triazole, C-5) and δ 145.61 ppm due to (1,2,4-triazole, C-3) confirmed the formation of compound **3**. The compound **3** on condensation with various aromatic aldehydes yielded 4-arylideneamino-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles **4a-j**. Formation of compounds **4a-j** was evidenced by the appearance of peaks at δ 8.62-8.69 ppm due to $\text{N}=\text{CH}$ and IR bands at 1625-1632 cm^{-1} for $-\text{N}=\text{CH}$ of arylidenes. Furthermore in the ^{13}C NMR spectra peaks were observed in the range of δ 143.1-144.9 ppm due to $-\text{N}=\text{CH}$ group, which confirmed the formation of compounds **4a-j**. The compounds **4a-j** on reaction with thioglycolic acid underwent dehydrative annulation afforded 4-(2-aryl-4-oxo-1,3-thiazolidine)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles **5a-j** (Scheme-1). Formation of the compounds **5a-j** was confirmed by the appearance of peaks at δ 3.40-3.48 ppm appeared due to CH_2 in the thiazolidine ring. In the IR spectra bands at 1720-1728 cm^{-1} for $>\text{C}=\text{O}$, cyclic were also observed. Furthermore in the ^{13}C NMR spectra peaks at δ 44.1-44.9 ppm were appeared due to $\text{S}-\text{CH}_2$ and peaks at δ 170.1-170.7 ppm were observed due to $>\text{C}=\text{O}$, cyclic confirmed the formation of compounds **5a-j**.

Table 1 Comparison of conventional and microwave synthesis for **4a-j** and **5a-j**

Compd	P ^a /watt	Temp. (in °C)	Conventional		Microwave		M.P. (in °C)
			Yield (%)	Time (hrs)	Yield (%)	Time (min)	
4a	200	80	72	2	85	3	160-161
4b	200	80	80	2	93	2	164-165
4c	200	80	81	2	94	1.5	168-169
4d	200	84	75	2.5	90	2	175-176
4e	200	80	77	2	91	2	177-178
4f	200	70	82	1	95	1	200-201
4g	200	70	84	1	96	1.5	205-206
4h	200	83	73	2.5	86	2.5	211-212
4i	200	90	75	3	88	2.5	213-214
4j	200	92	72	3	85	3	190-191
5a	200	94	70	3	83	4.5	183-184
5b	200	93	73	3	86	3.5	170-171
5c	200	92	74	3	87	3	175-176
5d	200	95	71	3.5	84	4	172-173
5e	200	100	72	4	85	4	178-179
5f	200	90	76	3	88	3	190-191
5g	200	85	79	2.5	90	3	192-193
5h	200	110	73	4	84	4	200-201
5i	200	108	74	4	87	4	203-204
5j	200	115	72	4.5	84	5	207-208

^a Microwave irradiation power

All the reactions under microwave irradiation were completed within 1-4.5 min whereas similar reactions under conventional heating (steam bath) at reflux gave poor yields after much longer reaction times. The impacts of microwave irradiation and conventional heating for the synthesis of compounds 4a-j and 5a-j have been compared. The results are summarized in **Table 1**.

Biological activity

All the final synthesized compounds **5a-j** were screened for their antibacterial activity against two different strains of Gram negative (*Escherichia coli* and *Salmonella typhi*) and Gram positive (*Streptococcus aureus* and *Bacillus subtilis*) bacteria, antifungal activity against *Aspergillus flavus*, *Aspergillus fumigates*, *Candida albicans* and *Fusarium oxysporum*. The antitubercular activity was screened against *Mycobacterium tuberculosis* H37Rv strain. Minimum inhibitory concentration (MIC) values of the compounds **5a-j** were determined using filter paper disc diffusion method for antibacterial and antifungal activities and L.J. medium method.²⁰ Standard antibacterial Streptomycin and antifungal Griseofulvin were also tested under the similar conditions for comparison. For the antitubercular activity Isoniazid and Rifampicin were used as standard and also screened under the similar conditions. Results of all given activities of compounds were given in **Table 2**.

Table 2 Antibacterial, antifungal and antitubercular activity of the compounds **5a-j** (MIC µg/ml)

Comp	<i>E. coli</i>	<i>S. typhi</i>	<i>B. subtilis</i>	<i>S. aureus</i>	<i>A. flavus</i>	<i>F. oxysporum</i>	<i>A. fumigats</i>	<i>C. albicans</i>	<i>M. tuberculosis</i>
5a	4.50	5.12	6.25	6.75	15.1	9.95	13.5	7.30	3.75
5b	1.62	2.25	2.75	3.50	13.5	9.30	12.5	6.90	2.75
5c	1.62	1.90	2.75	3.25	13.5	9.25	12.2	6.75	2.82
5d	2.80	3.25	4.12	5.25	14.2	9.32	13.2	7.25	3.25
5e	2.93	3.25	5.56	5.30	14.6	9.32	13.1	7.25	3.12
5f	1.35	1.62	2.25	2.56	13.2	9.16	11.5	6.45	2.75
5g	1.32	1.55	2.25	2.52	12.9	9.11	11.2	6.38	2.60
5h	6.25	7.20	7.88	7.94	16.0	10.1	13.6	7.75	3.75
5i	7.25	8.10	8.50	8.88	16.8	10.5	13.9	8.12	3.90
5j	8.20	9.25	9.30	9.95	17.5	11.2	14.2	8.15	3.94
Sm^a	1.25	1.50	2.20	2.50	-	-	-	-	-
Gf^b	-	-	-	-	12.5	8.25	10.5	6.25	-
Rf^c	-	-	-	-	-	-	-	-	2.50
In^d	-	-	-	-	-	-	-	-	1.25

^aStreptomycin, ^bGriseofulvin, ^cRifampicin, ^d Isoniazid

The results of the antimicrobial screening data revealed that all the compounds **5a-j** showed considerable and varied activity against the selected microorganism. Structure activity relationship (SAR) study of the substitution pattern of the aryl group towards antibacterial and antifungal activity have shown that electron withdrawing and donating groups causes, respectively more and less activity. The compounds **5f** and **5g** showed the maximum antibacterial activity (MIC 1.35 and 1.32 µg/ml) against *E.coli* and antifungal activity (MIC 6.45 and 6.38 µg/ml) against *Candida albicans*. The compounds **5f** and **5g** in which a nitro group is present at ortho and meta positions of

the aryl ring, respectively possess stronger antibacterial and antifungal activity than others. The compounds **5b**, **5c**, **5d** and **5e** (halo substituents) having a less electron withdrawing groups shows less antibacterial and antifungal activity as compared to **5f** and **5g**. The unsubstituted benzene has shown less antibacterial and antifungal activity as compared to nitro and halo substituents. The compounds **5h**, **5i** and **5j** shows very less antibacterial and antifungal activity as compared to others because of the presence of the electron donating groups such as methoxy and methyl. The sequence of the activity is in the following: $\text{NO}_2 > \text{Cl} > \text{Br} > \text{OCH}_3 > \text{CH}_3$

As seen from data of **Table 2**, most of the synthesized compounds generally possess very good antimycobacterial activity with MIC values in the range of 2.60-3.94 $\mu\text{g}/\text{ML}$. Best activity against *M.tuberculosis* H37Rv was observed for the 3-nitro substituted thiazolidine derivatives **5g**, which is only slightly less potent than the standard drug Rifampicin. The 2-nitro, 2,4-chloro and 2,3-bromo substituted thiazolidine derivatives **5f**, **5b**, **5c**, **5d**, **5e** shows less activity as compared to 3-nitro substituent derivative. Rest of the compounds showed lesser activity.

Conclusion

In conclusion, a series of 4-(2-aryl-4-oxo-1,3-thiazolidine)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (**5a-j**) derivatives were prepared by conventional as well as microwave method and screened for their antibacterial activity against three different strains, antifungal activity against three strains of fungi and antitubercular activity against *mycobacterium tuberculosis* H37Rv strain. Bioassay indicated that the compounds **5b**, **5c**, **5f**, **5g** were excellently active against all the strains and the remaining compounds showed good to moderate activity comparable with standard drugs. On the bases of structure-activity-relationship study of the compounds, it can be concluded that the presence of chloro/nitro group in the thiazolidine moiety enhanced the activity of the compounds.

Experimental section

Melting points were taken in open capillary tubes. Progress of the reaction was monitored by silica gel-G coated TLC plates using CHCl_3 : MeOH (9:1) system. The spots were exposed to iodine vapours for visualization. IR spectra were recorded on Shimadzu 8201 PC FTIR spectrophotometer (ν_{max} in cm^{-1}); ^1H NMR and ^{13}C NMR spectra were measured on Bruker DRX-300 spectrometer in CDCl_3 at 300 and 100 MHz, respectively using TMS as an internal standard. All chemical shifts are reported on δ scale. The FAB mass spectra were recorded on a Jeol SX 102 mass spectrometer. Elemental analysis was performed on a Carlo Erba 1108 analyzer providing satisfactory results. For column chromatographic purification of the products Merck Silica Gel 60 (230-400 Mesh) was used. The reagent grade chemicals were purchased from the commercial sources and further purified before use. Microwave assisted reactions were carried out in a QPro-M Modified Microwave Oven. In this unit, microwaves are generated by magnetron at a frequency of 2450 MHz having an output energy range of 100 to 800W and individual sensor for temperature control.

Synthesis of N-(ethyl ethanoate)-5-nitroindazole (1)

Conventional method

Equimolar solution of 5-nitroindazole (30g, 0.18 mol) and ethyl chloroacetate (22.55 g, 0.18 mol) in acetone (100 ml) was stirred for about 2 hr. The product was filtered and the solvent was evaporated to dryness in vacuo. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (7:3 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by acetone to give compound **1**. Yield 78%; m.p. 264-266°C; IR [ν , cm^{-1} , KBr]: 3046 (C-H, Ar-H), 1730 ($>\text{C}=\text{O}$, ester), 1601 (N=CH-, cyclic), 1530,1338 (ArNO₂), 1430 (N-CH₂); ^1H NMR [400 MHz, CDCl_3]: δ 7.90 (s, 1H, N=CH-, cyclic), 7.26-7.60 (m, 3H, Ar-H), 4.25 (q, 2H, J=7 Hz, $\text{COOCH}_2\text{CH}_3$), 2.51 (s, 2H, N-CH₂), 1.25 (t, 3H, J=7 Hz, $\text{COOCH}_2\text{CH}_3$); ^{13}C NMR [100 MHz, CDCl_3]: δ 168.9 (CO-O), 142.0 (C-NO₂, aromatic), 135.0 (N=CH-, cyclic),

110.9-122.2 (C of aromatic ring), 61.1 ($\underline{\text{CH}_2}$ $\underline{\text{CH}_3}$), 33.3 (N- $\underline{\text{CH}_2}$), 14.5 ($\underline{\text{CH}_2}$ $\underline{\text{CH}_3}$); Mass (m/z) : 249 [M]⁺, 204, 203, 176, 162, 134, 88; Anal. (%) for C₁₁H₁₁N₃O₄, Calcd. C, 53.01; H, 4.42; N, 16.87. Found: C, 52.98; H, 4.39; N, 16.83.

Microwave method

A mixture of 5-nitroindazole (30 g, 0.18 mol) and ethyl chloroacetate (22.55 g, 0.18 mol) were placed in a round bottom flask inside a microwave oven and irradiated (200 W, 76-78°C) for 2 min. The completion of the reaction was monitored by TLC. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (7:3 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by acetone to give compound **1**. Yield 90%; m.p. 264-266°C. Spectral and analytical data were found to similar as reported for conventional method.

Synthesis of N-(acetyl hydrazino)-5-nitroindazole (2)

Conventional method

Equimolar solution of the compound **1** (27g, 0.11 mol) and hydrazine hydrate (5.43 g, 0.11 mol) in dioxane (90 ml) was stirred for about 8 hr. The product was filtered and the solvent was evaporated to dryness in vacuo. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (7:3 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by acetone to give compound **2**. Yield 80%; m.p. 210-211°C; IR (v, cm⁻¹, KBr) : 3252, 3378 (-NHNH₂), 3045 (C-H, Ar-H), 1678 (>C=O, amide), 1600 (N=CH-, cyclic), 1527,1333 (ArNO₂), 1427 (N-CH₂); ¹HNMR [400 MHz, CDCl₃] : δ 8.20 (s, 1H, CONH), 7.89 (s, 1H, N=CH-, cyclic), 7.25-7.61 (m, 3H, Ar-H), 4.45 (s, 2H, NH₂), 2.49 (s, 2H, N-CH₂); ¹³CNMR [100 MHz, CDCl₃] : δ 168.0 (CONH), 142.2 (C-NO₂, aromatic), 135.2 (N=CH-, cyclic), 111.9-122.0 (C of aromatic ring), 33.5 (N-CH₂); Mass (m/z) : 235[M]⁺, 204, 189, 176, 162, 134, 88; Anal. (%) for C₉H₉N₅O₃, Calcd. C, 45.96; H, 3.83 ; N, 29.79. Found: C, 45.90 ; H, 3.79; N, 29.76.

Microwave method

A mixture of compound **1** (27g, 0.11 mol) and hydrazine hydrate (5.43 g, 0.11 mol) were placed in a round bottom flask inside a microwave oven and irradiated (200 W, 76-78°C) for 3.5 min. The completion of the reaction was monitored by TLC. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (7:3 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by acetone to give compound **2**. Yield 91%; m.p. 210-211°C. Spectral and analytical data were found to similar as reported for conventional method.

Synthesis of 4-amino-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazole (3)

Conventional method

Equimolar solution of the compound **2** (25g, 0.11 mol) and carbon disulphide (8.08g, 0.11mol) in the presence of ethanolic potassium hydroxide was stirred for about 3 hr. followed by treatment with hydrazine hydrate (5.32 g, 0.11 mol) in acetone (90 ml) was stirred for about 2 hr. The product was filtered and the solvent was evaporated to dryness in vacuo. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (8:2 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by acetone to give compound **3**. Yield 75%; m.p. 180-181°C; IR (v, cm⁻¹, KBr) : 3040 (C-H, Ar-H), 1678 (>C=O, amide), 1602 (N=CH-, cyclic), 1522,1336 (ArNO₂), 1430 (N-CH₂), 3204, 3305 (NH₂), 2581(-SH), 1614 (>C=N); ¹HNMR [300 MHz, CDCl₃] : δ 7.84 (s, 1H, N=CH-, cyclic), 7.20-7.62 (m, 3H, Ar-H), 5.51 (s, 2H, NH₂), 2.52 (s, 2H, N-CH₂), 13.60 (s, 1H, -SH); ¹³CNMR [100 MHz, CDCl₃] : δ 142.3 (C-NO₂, aromatic), 135.3 (N=CH-, cyclic), 112.4-122.3 (C of aromatic ring), 33.4 (N-CH₂), 152.70 (1,2,4-triazole, C-5), 145.61 (1,2,4-triazole, C-3);

Mass (m/z) : 291[M]⁺, 258, 245, 230, 217, 214, 201, 176, 169, 134, 115, 88, 87, 71; Anal. (%) for C₁₀H₉N₇O₂S, Calcd. C, 41.24; H, 3.09 ; N, 33.68. Found: C, 41.22 ; H, 3.06; N, 33.66.

Microwave method

A mixture of compound **2** (25g, 0.11 mol) and carbon disulphide (8,08g, 0.11 mol) in the presence of ethanolic potassium hydroxide were placed in a round bottom flask inside a microwave oven and irradiated (200 W, 76-78°C) for 2.5 min. followed by treatment with hydrazine hydrate (5.43 g, 0.11 mol) and irradiated (200 W, 76-78°C) for 3 min. The completion of the reaction was monitored by TLC. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (8:2 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by acetone to give compound **3a**. Yield 87%; m.p. 180-181°C. Spectral and analytical data were found to similar as reported for conventional method.

Synthesis of 4-benzylidene amino-5-mercapto-3- (5-nitroindazolyl methyl)-1,2,4-triazoles (4a)

Conventional method

Equimolar solution of the compound **3** (1.8 g, 0.006 mol) and benzaldehyde (0.65 g, 0.006 mol) in dioxane (30 ml) was stirred for about 2 hr. The product was filtered and the solvent was evaporated to dryness in vacuo. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (8:2 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by chloroform to give compound **4a**. Yield 72%; m.p. 160-161°C; IR [ν ,cm⁻¹, KBr] : 3042 (C-H, Ar-H), 1630 (N=CH-, acyclic), 1604 (N=CH-, cyclic), 1521,1333 (ArNO₂), 1428 (N-CH₂), 2580 (-SH), 1616 (>C=N). ¹HNMR [300 MHz, CDCl₃]: δ 8.67 (s, 1H, N=CH-, acyclic), 7.82 (s, 1H, N=CH-, cyclic), 7.22-7.62 (m, 8H, Ar-H) , 2.51 (s, 2H, N-CH₂), 13.62(s, 1H, -SH); ¹³CNMR [100 MHz, CDCl₃]: δ 143.8 (N=CH-, acyclic), 142.6 (C-NO₂, aromatic), 135.1 (N=CH-, cyclic), 112.2-122.2 (C of aromatic ring), 33.6 (N-CH₂), 152.72 (1,2,4-triazole, C-5), 145.61 (1,2,4-triazole, C-3); Mass (m/z): 379 [M]⁺, 346, 333, 318, 305, 214, 203, 201, 176, 175, 162, 134, 88, 71; Anal. (%) for C₁₇H₁₃N₇O₂S, Calcd. C, 53.83; H, 3.43; N, 25.86. Found: C, 53.81; H, 3.42; N, 25.82.

Microwave method

A mixture of the compound **3** (1.8 g, 0.006 mol) and benzaldehyde (0.65 g, 0.006 mol) were placed in a round bottom flask inside a microwave oven and irradiated (200 W, 80°C) for 3 min. The completion of the reaction was monitored by TLC. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (8:2 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by acetone to give compound **4a**. Yield 85%; m.p. 160-161°C. Spectral and analytical data were found to similar as reported for conventional method.

Other compounds **4b-j** were prepared similarly by treating **3** with various aromatic aldehydes.

4-(2-chlorobenzylidene amino)-5-mercapto-3- (5-nitroindazolyl methyl)-1,2,4-triazoles (4b)

IR [ν ,cm⁻¹, KBr] : 3045 (C-H, Ar-H), 1628 (N=CH-, acyclic), 1601 (N=CH-, cyclic), 1523,1331 (ArNO₂), 1432 (N-CH₂), 2582 (-SH), 1615 (>C=N), 750 (Ar-Cl). ¹HNMR [300 MHz, CDCl₃]: δ 8.66 (s, 1H, N=CH-, acyclic), 7.81 (s, 1H, N=CH-, cyclic), 7.21-7.61 (m, 7H, Ar-H) , 2.50 (s, 2H, N-CH₂), 13.62(-SH); ¹³CNMR [100 MHz, CDCl₃]: δ 143.7 (N=CH-, acyclic), 142.4 (C-NO₂, aromatic), 135.3 (N=CH-, cyclic), 112.5-122.1 (C of aromatic ring), 33.3 (N-CH₂), 152.71 (1,2,4-triazole, C-5), 145.63 (1,2,4-triazole, C-3), 133.7 (C-Cl, aromatic); Mass (m/z): 413.5 [M]⁺, 380.5, 367.5, 352.5, 339.5, 237.5, 214, 209.5, 201, 176, 162, 134, 88, 71. Anal. (%) for C₁₇H₁₂N₇O₂SCl, Calcd. C, 49.33; H, 2.90; N, 23.70. Found: C, 49.31; H, 2.87; N, 23.68.

4-(4-chlorobenzylidene amino)-5-mercapto-3- (5-nitroindazolyl methyl)-1,2,4-triazoles (4c)

IR [ν , cm^{-1} , KBr] : 3043 (C-H, Ar-H), 1630 (N=CH-, acyclic), 1602 (N=CH-, cyclic), 1522, 1335 (ArNO₂), 1431 (N-CH₂), 2584 (-SH), 1613 (>C=N), 752 (Ar-Cl). ¹HNMR [300 MHz, CDCl₃]: δ 8.64 (s, 1H, N=CH-, acyclic), 7.80 (s, 1H, N=CH-, cyclic), 7.25-7.60 (m, 7H, Ar-H), 2.54 (s, 2H, N-CH₂), 13.63 (s, 1H, -SH); ¹³CNMR [100 MHz, CDCl₃]: δ 143.9 (N=CH-, acyclic), 142.5 (C-NO₂, aromatic), 135.5 (N=CH-, cyclic), 112.2-122.1 (C of aromatic ring), 33.2 (N-CH₂), 152.70 (1,2,4-triazole, C-5), 145.62 (1,2,4-triazole, C-3), 133.9 (C-Cl, aromatic); Mass (m/z): 413.5 [M]⁺, 380.5, 367.5, 352.5, 339.5, 237.5, 214, 209.5, 201, 176, 162, 134, 88, 71; Anal. (%) for C₁₇H₁₂N₇O₂SCl, Calcd. C, 49.33; H, 2.90; N, 23.70. Found: C, 49.32; H, 2.88; N, 23.67.

4-(2-bromobenzylidene amino)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (4d)

IR [ν , cm^{-1} , KBr] : 3044 (C-H, Ar-H), 1630 (N=CH-, acyclic), 1600 (N=CH-, cyclic), 1524,1334 (ArNO₂), 1430 (N-CH₂), 2583 (-SH), 1616 (>C=N), 614 (Ar-Br). ¹HNMR [300 MHz, CDCl₃]: δ 8.63 (s, 1H, N=CH-, acyclic), 7.82 (s, 1H, N=CH-, cyclic), 7.21-7.62 (m, 7H, Ar-H), 2.52 (s, 2H, N-CH₂), 13.65 (s, 1H, -SH); ¹³CNMR [100 MHz, CDCl₃]: δ 143.6 (N=CH-, acyclic), 142.3 (C-NO₂, aromatic), 135.3 (N=CH-, cyclic), 112.2-122.1 (C of aromatic ring), 33.4 (N-CH₂), 152.74 (1,2,4-triazole, C-5), 145.64 (1,2,4-triazole, C-3), 118.2 (C-Br, aromatic); Mass (m/z): 458 [M]⁺, 425, 412, 397, 384, 282, 254, 214, 201, 176, 162, 134, 88, 71; Anal. (%) for C₁₇H₁₂N₇O₂SBr, Calcd. C, 44.55; H, 2.62; N, 21.40. Found: C, 44.52; H, 2.60; N, 21.39.

4-(3-bromobenzylidene amino)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (4e)

IR [ν , cm^{-1} , KBr] : 3042 (C-H, Ar-H), 1630 (N=CH-, acyclic), 1600 (N=CH-, cyclic), 1526,1338 (ArNO₂), 1432 (N-CH₂), 2582 (-SH), 1612 (>C=N), 617 (Ar-Br). ¹HNMR [300 MHz, CDCl₃]: δ 8.63 (s, 1H, N=CH-, acyclic), 7.82 (s, 1H, N=CH-, cyclic), 7.24-7.63 (m, 7H, Ar-H), 2.53 (s, 2H, N-CH₂), 13.69 (s, 1H, -SH); ¹³CNMR [100 MHz, CDCl₃]: δ 143.4 (N=CH-, acyclic), 142.7 (C-NO₂, aromatic), 135.4 (N=CH-, cyclic), 112.5-122.3 (C of aromatic ring), 33.7 (N-CH₂), 152.72 (1,2,4-triazole, C-5), 145.61 (1,2,4-triazole, C-3), 118.4 (C-Br, aromatic); Mass (m/z): 458 [M]⁺, 425, 412, 397, 384, 282, 214, 201, 176, 254, 162, 134, 88, 71; Anal. (%) for C₁₇H₁₂N₇O₂SBr, Calcd. C, 44.55; H, 2.62; N, 21.40. Found: C, 44.53; H, 2.61; N, 21.39.

4-(2-nitrobenzylidene amino)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (4f)

IR [ν , cm^{-1} , KBr] : 3041 (C-H, Ar-H), 1632 (N=CH-, acyclic), 1605 (N=CH-, cyclic), 1523,1333 (ArNO₂), 1436 (N-CH₂), 2585 (-SH), 1616 (>C=N). ¹HNMR [300 MHz, CDCl₃]: δ 8.66 (s, 1H, N=CH-, acyclic), 7.85 (s, 1H, N=CH-, cyclic), 7.23-7.60 (m, 7H, Ar-H), 2.51 (s, 2H, N-CH₂), 13.66(s, 1H, -SH); ¹³CNMR [100 MHz, CDCl₃]: δ 143.7 (N=CH-, acyclic), 142.8 (C-NO₂, aromatic), 135.7 (N=CH-, cyclic), 112.4-122.3 (C of aromatic ring), 33.6 (N-CH₂), 152.73 (1,2,4-triazole, C-5), 145.62 (1,2,4-triazole, C-3); Mass (m/z): 424 [M]⁺, 391, 378, 363, 350, 248, 220, 214, 201, 176, 162, 134, 88, 71; Anal. (%) for C₁₇H₁₂N₈O₄S, Calcd. C, 48.11; H, 2.83; N, 26.42. Found: C, 48.10; H, 2.81; N, 26.40.

4-(4-nitrobenzylidene amino)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (4g)

IR [ν , cm^{-1} , KBr] : 3046 (C-H, Ar-H), 1628 (N=CH-, acyclic), 1601 (N=CH-, cyclic), 1525,1337 (ArNO₂), 1433 (N-CH₂), 2582 (-SH), 1617 (>C=N). ¹HNMR [300 MHz, CDCl₃]: δ 8.66 (s, 1H, N=CH-, acyclic), 7.85 (s, 1H, N=CH-, cyclic), 7.22-7.61 (m, 7H, Ar-H), 2.54 (s, 2H, N-CH₂), 13.68 (s, 1H, -SH); ¹³CNMR [100 MHz, CDCl₃]: δ 144.4 (N=CH-, acyclic), 143.1 (C-NO₂, aromatic), 135.3 (N=CH-, cyclic), 112.1-122.5 (C of aromatic ring), 33.9 (N-CH₂), 152.76 (1,2,4-triazole, C-5), 145.64 (1,2,4-triazole, C-3); Mass (m/z): 424 [M]⁺, 391, 378, 363, 350, 248, 220, 214, 201, 176, 162, 134, 88, 71; Anal. (%) for C₁₇H₁₂N₈O₄S, Calcd. C, 48.11; H, 2.83; N, 26.42. Found: C, 48.09; H, 2.82; N, 26.39.

4-(2-methoxybenzylidene amino)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazole (4h)

IR [ν , cm^{-1} , KBr] : 3048 (C-H, Ar-H), 1625 (N=CH-, acyclic), 1604 (N=CH-, cyclic), 1529,1334 (ArNO₂), 1431 (N-CH₂), 2586 (-SH), 1619 (>C=N), 2822 (Ar-OCH₃). ¹HNMR [300 MHz, CDCl₃]: δ 8.68 (s, 1H, N=CH-, acyclic), 7.88 (s, 1H, N=CH-, cyclic), 7.21-7.61 (m, 7H, Ar-H), 2.52 (s, 2H, N-CH₂), 13.65 (s, 1H, -SH), 3.88 (s, 3H, OCH₃); ¹³CNMR [100 MHz, CDCl₃]: δ 144.2 (N=CH-, acyclic), 143.3 (C-NO₂, aromatic), 135.1 (N=CH-, cyclic), 112.3-

122.5 (C of aromatic ring), 33.8 (N-CH₂), 152.71 (1,2,4-triazole, C-5), 145.65 (1,2,4-triazole, C-3) 55.1 (OCH₃); Mass (m/z): 409 [M]⁺, 376, 363, 348, 335, 233, 214, 205, 201, 176, 162, 134, 88, 71; Anal. (%) for C₁₈H₁₅N₇O₃S, Calcd. C, 52.81; H, 3.67; N, 23.96. Found: C, 52.80; H, 3.64; N, 23.94.

4-(4-methoxybenzylidene amino)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazole (4i)

IR [ν,cm⁻¹, KBr] : 3047 (C-H, Ar-H), 1627 (N=CH-, acyclic), 1606 (N=CH-, cyclic), 1527,1338 (ArNO₂), 1430 (N-CH₂), 2584 (-SH), 1621 (>C=N), 2824 (Ar-OCH₃). ¹HNMR [300 MHz, CDCl₃]: δ 8.69 (s, 1H, N=CH-, acyclic), 7.86 (s, 1H, N=CH-, cyclic), 7.20-7.62 (m, 7H, Ar-H), 2.56 (s, 2H, N-CH₂), 13.69 (s, 1H, -SH), 3.90 (s, 3H, OCH₃); ¹³CNMR [100 MHz, CDCl₃]: δ 144.9 (N=CH-, acyclic), 142.8 (C-NO₂, aromatic), 135.4 (N=CH-, cyclic), 112.2-122.4 (C of aromatic ring), 33.4 (N-CH₂), 152.74 (1,2,4-triazole, C-5), 145.61 (1,2,4-triazole, C-3) 55.3 (OCH₃); Mass (m/z): 409 [M]⁺, 376, 363, 348, 335, 233, 214, 205, 201, 176, 162, 134, 88, 71; Anal. (%) for C₁₈H₁₅N₇O₃S, Calcd. C, 52.81; H, 3.67; N, 23.96. Found: C, 52.80; H, 3.65; N, 23.95.

4-(4-methylbenzylidene amino)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazole (4j)

IR [ν,cm⁻¹, KBr] : 3042 (C-H, Ar-H), 1630 (N=CH-, acyclic), 1603 (N=CH-, cyclic), 1530,1340 (ArNO₂), 1435 (N-CH₂), 2587 (-SH), 1620 (>C=N), 2921 (Ar-CH₃). ¹HNMR [300 MHz, CDCl₃]: δ 8.67 (s, 1H, N=CH-, acyclic), 7.90 (s, 1H, N=CH-, cyclic), 7.22-7.62 (m, 8H, Ar-H), 2.54 (s, 2H, N-CH₂), 13.60 (s, 1H, -SH), 2.30 (Ar-CH₃); ¹³CNMR [100 MHz, CDCl₃]: δ 144.8 (N=CH-, acyclic), 142.9 (C-NO₂, aromatic), 135.8 (N=CH-, cyclic), 112.3-122.6 (C of aromatic ring), 33.6 (N-CH₂), 152.77 (1,2,4-triazole, C-5), 145.63 (1,2,4-triazole, C-3), 22.6 (CH₃); Mass (m/z): 393 [M]⁺, 360, 347, 332, 319, 217, 214, 201, 189, 176, 162, 134, 88,71; Anal. (%) for C₁₈H₁₅N₇O₂S, Calcd. C, 54.96; H, 3.82; N, 24.94. Found: C, 54.93; H, 3.80; N, 24.92.

Synthesis of 4-(2-phenyl-4-oxo-1,3-thiazolidine)-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5a)

Conventional method

Equimolar solution of the compound **4a** (1.5g, 0.005 mol) and thioglycolic acid (0.43 g, 0.005 mol) with a pinch of anhydrous ZnCl₂ in acetone (25 ml) was stirred for about 4.5 hr. The product was filtered and the solvent was evaporated to dryness in vacuo. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (7:3 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by chloroform to give compound **5a**. Yield 70%; m.p. 183-184°C; IR [ν, cm⁻¹, KBr]: 3047 (C-H, Ar-H), 1607 (N=CH-, cyclic), 1528, 1335 (ArNO₂), 1432 (N-CH₂), 2583(-SH), 1621 (>C=N), 2980 (N-CH-S), 685 (C-S-C), 1720 (>C=O, cyclic). ¹HNMR [300 MHz, CDCl₃]: δ 7.86 (s, 1H, N=CH-, cyclic), 7.23-7.65 (m, 8H, Ar-H), 2.57 (s, 2H, N-CH₂), 13.63(s, 1H, -SH), 4.10 (s, 1H, -N-CH), 3.40 (s, 2H, CH₂, cyclic); ¹³CNMR [100 MHz, CDCl₃]: δ 142.6 (C-NO₂, aromatic), 135.9 (N=CH-, cyclic), 112.5-122.5 (C of aromatic ring), 34.1 (N-CH₂), 152.71 (1,2,4-triazole, C-5), 145.66 (1,2,4-triazole, C-3), 44.8 (CH₂ of thiazolidine ring), 40.2 (N-CH-S), 170.1 (>C=O, cyclic); Mass (m/z): 421 [M]⁺, 393, 388, 375, 365, 360, 351, 347, 332, 319, 318, 305, 245, 217, 189, 178, 176, 175, 162, 150, 136, 134, 88. Anal. (%) for C₁₉H₁₅N₇O₃S₂, Calcd. C, 54.16; H, 3.56; N, 23.28. Found: C, 54.14; H, 3.54; N, 23.27.

Microwave method

A mixture of the compound **4a** (1.5g, 0.005 mol) and thioglycolic acid (0.43 g, 0.005 mol) with a pinch of anhydrous ZnCl₂ were placed in a round bottom flask inside a microwave oven and irradiated (200 W, 94°C) for 3 min. The completion of the reaction was monitored by TLC. The crude product was readily purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (7:3 v/v) as eluant to obtain pure derivative. The resulting purified product was recrystallized by acetone to give compound **5a**. Yield 83%; m.p. 183-184°C. Spectral and analytical data were found to be similar as reported for conventional method. Other compounds such as **5b-j** were prepared similarly by using **4b-j** respectively.

4-{2-(2-chlorophenyl)-4-oxo-1,3-thiazolidine}-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5b)

IR [ν , cm^{-1} , KBr]: 3044 (C-H, Ar-H), 1610 (N=CH-, cyclic), 1531, 1334 (ArNO₂), 1428 (N-CH₂), 2580 (-SH), 1619 (>C=N), 2982 (N-CH-S), 688 (C-S-C), 1722 (>C=O, cyclic), 751 (Ar-Cl). ¹HNMR [300 MHz, CDCl₃]: δ 7.83 (s, 1H, N=CH-, cyclic), 7.21-7.64 (m, 7H, Ar-H), 2.53 (s, 2H, N-CH₂), 13.64 (s, 1H, -SH), 4.11 (s, 1H, -N-CH), 3.42 (s, 2H, CH₂, cyclic); ¹³CNMR [100 MHz, CDCl₃]: δ 142.8 (C-NO₂, aromatic), 135.6 (N=CH-, cyclic), 112.6-122.2 (C of aromatic ring), 34.3 (N-CH₂), 152.73 (1,2,4-triazole, C-5), 145.68 (1,2,4-triazole, C-3), 44.6 (CH₂ of thiazolidine ring), 40.4 (N-CH-S), 170.2 (>C=O, cyclic), 134.1 (C-Cl, aromatic); Mass (m/z): 455.5 [M]⁺, 427.5, 422.5, 409.5, 399.5, 394.5, 385.5, 381.5, 366.5, 353.5, 352.5, 339.5, 279.5, 251.5, 223.5, 212.5, 209.5, 184.5, 176, 170.5, 162, 134, 88. Anal. (%) for C₁₉H₁₄N₇O₃S₂Cl, Calcd. C, 50.05; H, 3.07; N, 21.51. Found: C, 50.02; H, 3.05; N, 21.47.

4-{2-(4-chlorophenyl)-4-oxo-1,3-thiazolidine}-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5c)

IR [ν , cm^{-1} , KBr]: 3048 (C-H, Ar-H), 1608 (N=CH-, cyclic), 1529, 1336 (ArNO₂), 1426 (N-CH₂), 2584 (-SH), 1618 (>C=N), 2981 (N-CH-S), 686 (C-S-C), 1721 (>C=O, cyclic), 754 (Ar-Cl). ¹HNMR [300 MHz, CDCl₃]: δ 7.82 (s, 1H, N=CH-, cyclic), 7.22-7.62 (m, 7H, Ar-H), 2.55 (s, 2H, N-CH₂), 13.60 (s, 1H, -SH), 4.13 (s, 1H, -N-CH), 3.41 (s, 2H, CH₂, cyclic); ¹³CNMR [100 MHz, CDCl₃]: δ 142.7 (C-NO₂, aromatic), 135.7 (N=CH-, cyclic), 112.4-122.3 (C of aromatic ring), 34.2 (N-CH₂), 152.76 (1,2,4-triazole, C-5), 145.65 (1,2,4-triazole, C-3), 44.3 (CH₂ of thiazolidine ring), 40.1 (N-CH-S), 170.3 (>C=O, cyclic), 134.3 (C-Cl, aromatic); Mass (m/z): 455.5 [M]⁺, 427.5, 422.5, 409.5, 399.5, 394.5, 385.5, 381.5, 360.5, 353.5, 352.5, 339.5, 279.5, 251.5, 223.5, 212.5, 209.5, 184.5, 176, 170.5, 162, 134, 88. Anal. (%) for C₁₉H₁₄N₇O₃S₂Cl, Calcd. C, 50.05; H, 3.07; N, 21.51. Found: C, 50.04; H, 3.05; N, 21.49.

4-{2-(2-bromophenyl)-4-oxo-1,3-thiazolidine}-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5d)

IR [ν , cm^{-1} , KBr]: 3051 (C-H, Ar-H), 1602 (N=CH-, cyclic), 1528, 1333 (ArNO₂), 1429 (N-CH₂), 2581 (-SH), 1622 (>C=N), 2984 (N-CH-S), 687 (C-S-C), 1724 (>C=O, cyclic), 616 (Ar-Br). ¹HNMR [300 MHz, CDCl₃]: δ 7.85 (s, 1H, N=CH-, cyclic), 7.23-7.65 (m, 7H, Ar-H), 2.51 (s, 2H, N-CH₂), 13.63 (s, 1H, -SH), 4.12 (s, 1H, -N-CH), 3.43 (s, 2H, CH₂, cyclic); ¹³CNMR [100 MHz, CDCl₃]: δ 142.5 (C-NO₂, aromatic), 136.1 (N=CH-, cyclic), 112.4-122.5 (C of aromatic ring), 34.1 (N-CH₂), 152.75 (1,2,4-triazole, C-5), 145.61 (1,2,4-triazole, C-3), 44.1 (CH₂ of thiazolidine ring), 40.3 (N-CH-S), 170.6 (>C=O, cyclic), 118.5 (C-Br, aromatic); Mass (m/z): 500 [M]⁺, 472, 467, 454, 444, 439, 430, 426, 411, 398, 397, 384, 324, 296, 268, 257, 254, 229, 215, 176, 162, 134, 88. Anal. (%) for C₁₉H₁₄N₇O₃S₂Br, Calcd. C, 45.61; H, 2.80; N, 19.60. Found: C, 45.60; H, 2.78; N, 19.58.

4-{2-(3-bromophenyl)-4-oxo-1,3-thiazolidine}-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5e)

IR [ν , cm^{-1} , KBr]: 3049 (C-H, Ar-H), 1604 (N=CH-, cyclic), 1530, 1331 (ArNO₂), 1430 (N-CH₂), 2585 (-SH), 1620 (>C=N), 2983 (N-CH-S), 685 (C-S-C), 1722 (>C=O, cyclic), 613 (Ar-Br). ¹HNMR [300 MHz, CDCl₃]: δ 7.81 (s, 1H, N=CH-, cyclic), 7.21-7.64 (m, 7H, Ar-H), 2.54 (s, 2H, N-CH₂), 13.66 (s, 1H, -SH), 4.14 (s, 1H, -N-CH), 3.42 (s, 2H, CH₂, cyclic); ¹³CNMR [100 MHz, CDCl₃]: δ 142.9 (C-NO₂, aromatic), 136.3 (N=CH-, cyclic), 112.3-122.6 (C of aromatic ring), 34.3 (N-CH₂), 152.74 (1,2,4-triazole, C-5), 145.66 (1,2,4-triazole, C-3), 44.4 (CH₂ of thiazolidine ring), 40.5 (N-CH-S), 170.4 (>C=O, cyclic), 118.3 (C-Br, aromatic); Mass (m/z): 500 [M]⁺, 472, 467, 454, 444, 439, 430, 426, 411, 398, 397, 384, 324, 296, 268, 257, 254, 229, 215, 176, 162, 134, 88. Anal. (%) for C₁₉H₁₄N₇O₃S₂Br, Calcd. C, 45.61; H, 2.80; N, 19.60. Found: C, 45.60; H, 2.79; N, 19.58.

4-{2-(2-nitrophenyl)-4-oxo-1,3-thiazolidine}-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5f)

IR [ν , cm^{-1} , KBr]: 3046 (C-H, Ar-H), 1603 (N=CH-, cyclic), 1527, 1336 (ArNO₂), 1434 (N-CH₂), 2583 (-SH), 1621 (>C=N), 2982 (N-CH-S), 688 (C-S-C), 1723 (>C=O, cyclic). ¹HNMR [300 MHz, CDCl₃]: δ 7.83 (s, 1H, N=CH-, cyclic), 7.20-7.63 (m, 7H, Ar-H), 2.58 (s, 2H, N-CH₂), 13.70 (-SH), 4.11 (s, 1H, -N-CH), 3.44 (s, 2H, CH₂, cyclic); ¹³CNMR [100 MHz, CDCl₃]: δ 142.4 (C-NO₂, aromatic), 136.2 (N=CH-, cyclic), 112.1-122.3 (C of aromatic ring), 34.2 (N-CH₂), 152.75 (1,2,4-triazole, C-5), 145.64 (1,2,4-triazole, C-3), 44.9 (CH₂ of thiazolidine ring), 40.4 (N-CH-S), 170.5 (>C=O, cyclic); Mass (m/z): 466 [M]⁺, 438, 433, 420, 410, 405, 396, 392, 377, 364, 363, 350, 290, 262, 234, 223, 220, 195, 181, 176, 162, 134, 88. Anal. (%) for C₁₉H₁₄N₈O₅S₂, Calcd. C, 48.93; H, 3.00; N, 24.03. Found: C, 48.90; H, 2.98; N, 24.01.

4-{2-(3-nitrophenyl)-4-oxo-1,3-thiazolidine}-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5g)

IR [ν , cm^{-1} , KBr]: 3045 (C-H, Ar-H), 1601 (N=CH-, cyclic), 1531, 1337 (ArNO₂), 1433 (N-CH₂), 2582 (-SH), 1619 (>C=N), 2985 (N-CH-S), 690 (C-S-C), 1728 (>C=O, cyclic). ¹HNMR [300 MHz, CDCl₃]: δ 7.86 (s, 1H, N=CH-, cyclic), 7.22-7.62 (m, 7H, Ar-H), 2.56 (s, 2H, N-CH₂), 13.72 (s, 1H, -SH), 4.13 (s, 1H, -N-CH), 3.46 (s, 2H, CH₂, cyclic); ¹³CNMR [100 MHz, CDCl₃]: δ 143.2 (C-NO₂, aromatic), 136.4 (N=CH-, cyclic), 112.4-122.7 (C of aromatic ring), 34.5 (N-CH₂), 152.79 (1,2,4-triazole, C-5), 145.67 (1,2,4-triazole, C-3), 44.6 (CH₂ of thiazolidine ring), 40.8 (N-CH-S), 170.6 (>C=O, cyclic); Mass (m/z): 466 [M]⁺, 438, 433, 420, 410, 405, 396, 392, 377, 364, 363, 350, 290, 262, 234, 223, 220, 195, 181, 176, 162, 134, 88. Anal. (%) for C₁₉H₁₄N₈O₅S₂, Calcd. C, 48.93; H, 3.00; N, 24.03. Found: C, 48.91; H, 2.99; N, 24.02.

4-{2-(2-methoxyphenyl)-4-oxo-1,3-thiazolidine}-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5h)

IR [ν , cm^{-1} , KBr]: 3052 (C-H, Ar-H), 1605 (N=CH-, cyclic), 1528, 1334 (ArNO₂), 1431 (N-CH₂), 2584 (-SH), 1618 (>C=N), 2988 (N-CH-S), 687 (C-S-C), 1727 (>C=O, cyclic), 2823 (Ar-OCH₃). ¹HNMR [300 MHz, CDCl₃]: δ 7.88 (s, 1H, N=CH-, cyclic), 7.24-7.64 (m, 7H, Ar-H), 2.53 (s, 2H, N-CH₂), 13.71 (s, 1H, -SH), 4.11 (s, 1H, -N-CH), 3.45 (s, 2H, CH₂, cyclic), 3.89 (s, 3H, OCH₃); ¹³CNMR [100 MHz, CDCl₃]: δ 143.3 (C-NO₂, aromatic), 136.3 (N=CH-, cyclic), 112.8-122.2 (C of aromatic ring), 34.1 (N-CH₂), 152.80 (1,2,4-triazole, C-5), 145.69 (1,2,4-triazole, C-3), 44.4 (CH₂ of thiazolidine ring), 40.6 (N-CH-S), 170.4 (>C=O, cyclic), 55.2 (OCH₃); Mass (m/z): 451 [M]⁺, 423, 418, 405, 395, 390, 381, 377, 362, 349, 348, 335, 275, 247, 219, 208, 205, 180, 176, 166, 162, 134, 88. Anal. (%) for C₂₀H₁₇N₇O₄S₂, Calcd. C, 53.22; H, 3.77; N, 21.73. Found: C, 53.20; H, 3.74; N, 21.70.

4-{2-(4-methoxyphenyl)-4-oxo-1,3-thiazolidine}-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5i)

IR [ν , cm^{-1} , KBr]: 3054 (C-H, Ar-H), 1609 (N=CH-, cyclic), 1529, 1338 (ArNO₂), 1428 (N-CH₂), 2586 (-SH), 1617 (>C=N), 2986 (N-CH-S), 687 (C-S-C), 1728 (>C=O, cyclic), 2826 (Ar-OCH₃). ¹HNMR [300 MHz, CDCl₃]: δ 7.87 (s, 1H, N=CH-, cyclic), 7.29-7.62 (m, 7H, Ar-H), 2.55 (s, 2H, N-CH₂), 13.69 (s, 1H, -SH), 4.12 (s, 1H, -N-CH), 3.44 (s, 2H, CH₂, cyclic), 3.91 (s, 3H, OCH₃); ¹³CNMR [100 MHz, CDCl₃]: δ 143.5 (C-NO₂, aromatic), 136.5 (N=CH-, cyclic), 112.7-122.4 (C of aromatic ring), 34.3 (N-CH₂), 152.78 (1,2,4-triazole, C-5), 145.62 (1,2,4-triazole, C-3), 44.3 (CH₂ of thiazolidine ring), 40.9 (N-CH-S), 170.7 (>C=O, cyclic), 55.6 (OCH₃); Mass (m/z): 451 [M]⁺, 423, 418, 405, 395, 390, 381, 377, 362, 349, 348, 335, 275, 247, 219, 208, 205, 180, 176, 166, 162, 134, 88. Anal. (%) for C₂₀H₁₇N₇O₄S₂, Calcd. C, 53.22; H, 3.77; N, 21.73. Found: C, 53.20; H, 3.75; N, 21.71.

4-{2-(4-methylphenyl)-4-oxo-1,3-thiazolidine}-5-mercapto-3-(5-nitroindazolyl methyl)-1,2,4-triazoles (5j)

IR [ν , cm^{-1} , KBr]: 3053 (C-H, Ar-H), 1610 (N=CH-, cyclic), 1532, 1340 (ArNO₂), 1432 (N-CH₂), 2583 (-SH), 1615 (>C=N), 2990 (N-CH-S), 689 (C-S-C), 1725 (>C=O, cyclic), 2923 (Ar-CH₃). ¹HNMR [300 MHz, CDCl₃]: δ 7.84 (s, 1H, N=CH-, cyclic), 7.28-7.62 (m, 7H, Ar-H), 2.54 (s, 2H, N-CH₂), 13.66 (-SH), 4.14 (s, 1H, -N-CH), 3.48 (s, 2H, CH₂, cyclic), 2.31 (s, 3H, Ar-CH₃); ¹³CNMR [100 MHz, CDCl₃]: δ 143.1 (C-NO₂, aromatic), 136.4 (N=CH-, cyclic), 112.1-122.9 (C of aromatic ring), 34.2 (N-CH₂), 152.81 (1,2,4-triazole, C-5), 145.61 (1,2,4-triazole, C-3), 44.2 (CH₂ of thiazolidine ring), 40.7 (N-CH-S), 170.1 (>C=O, cyclic), 22.5 (CH₃); Mass (m/z): 435 [M]⁺, 407, 402, 389, 379, 365, 361, 346, 333, 332, 319, 262, 259, 203, 192, 189, 176, 164, 162, 150, 134, 88. Anal. (%) for C₂₀H₁₇N₇O₃S₂, Calcd. C, 55.17; H, 3.91; N, 22.53. Found: C, 55.14; H, 3.90; N, 22.51.

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