Research Article

Environ-Economic Synthesis and Characterization of Some New 1,2,4-Triazole Derivatives as Organic Fluorescent Materials and Potent Fungicidal Agents

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A multicomponent one-pot clean cyclocondensation reaction of 4-chloro-2-nitro aniline/amino acids and aromatic aldehydes/indole-2,3-diones with thiosemicarbazide in water yielding triazole/spiro indole-triazole derivatives in high yields and shorter reaction time and displaying excellent florescent property is reported. The developed MCR may provide a valuable practical tool for the synthesis of new drugs containing the title core fragment. All the newly synthesized compounds have been characterized by IR, ^1H NMR, ^{13}C NMR, and fluorescence study and also been screened for antimicrobial activity.

1. Introduction

Multicomponent and domino reactions are efficient and effective methods in the sustainable and diversity-oriented synthesis of heterocycles and such reactions have attracted enormous interest in recent years [1]. Thiosemicarbazide and its derivatives are an important class of synthetic compounds, having large variety of applications due to their wide spectrum of biological activities [2] including antiviral [3] and antitumoral [4] as well as parasitocidal activity against *Plasmodium falciparum*, *Plasmodium berghei* [5], *Trypanosoma cruzi* [6–8] *Trypanosoma brucei rhodesiense* [9], and *Toxoplasma gondii* [10].

The 1,2,4-triazoles and their derivatives are found to be associated with various biological activities such as anti-convulsant [11], antifungal [12], anticancer [13], antiinflammatory [14], and antibacterial properties [15]. Also several compounds containing 1,2,4-triazole rings are well known as drugs; for example, fluconazole is used as an antimicrobial drug, while vorozole, letrozole, and anastrozole are nonsteroidal drugs used for the treatment of cancer.

The increasing diversity of small molecule libraries is an important source for the discovery of new drug candidates.

In terms of this trend, the literature survey showed that indole derivatives possess anticancer [16, 17], antioxidant [18], antibacterial [19], antifungal [20, 21], antiviral [22, 23], and antihypertensive activities [24]. Indole-3-carbon atom in the form of spiro carbon atom exhibits enhanced biological activities [25, 26].

The important biological activities of triazole derivatives impelled us to take up the synthesis of these new combination heterocycles which are likely to have augmented diverse biological activity. The developed MCR may provide a valuable practical tool for the synthesis of novel physiologically active agents containing the title core fragment. Several methods [27–30] for the synthesis of 1,2,4-triazole derivatives are reported in the literature but all these methods require the presence of organic solvents and also require long reaction time. Further, there are only few reports [31–33] available in the literature regarding the synthesis of triazole derivatives under environmentally benign conditions. Earlier we also reported [33] the synthesis of spiro indole-triazoles under microwaves using montmorillonite as an inorganic solid support.

In recent years, organic research is mainly focused on the development of greener and environ-economic methods

SCHEME 1: Synthesis of triazole derivatives **4** and **5**.

which involve use of alternative reaction media to replace volatile and hazardous solvents like benzene, toluene, and methanol, commonly used in organic synthesis. Nowadays, many organic transformations have been carried out in water [34–38]. It is a unique solvent because it is readily available, inexpensive, nontoxic, safer, and environmentally benign.

Recently, triazole-based fluorescent sensors have been developed for the selective detection of platinum ions in aqueous solutions [38] and synthesis of a pyrenyl-appended triazole-based calyx[4]arene [39] as a fluorescent sensor for Cd^{+2} and Zn^{+2} is carried out. Prompted by rapidly expanding applications of organic fluorescent materials for electroluminescence (EL), dyelasers, sensors, probes, and phototherapeutic agents, and in view of the fluorescent properties associated with triazole derivatives, development of new fluorescent organic compounds with high functionality has been the subject of intense study for more than a decade [40–43].

In this context, we have synthesized new 1,2,4-triazole derivatives (4/5) using water as a green solvent under the umbrella of green chemistry and synthesized compounds have been evaluated for antibacterial and antifungal activity and also fluorescent properties.

2. Result and Discussion

In continuation of our work to develop greener and expeditious protocols for the synthesis of heterocyclic compounds [44–48], herein we wish to report a highly efficient procedure for the synthesis of new substituted-2*H*-1,2,4-triazole phenol derivatives (**4**) and spiro (indole-triazole) propanoic acid derivatives (**5**) using water (containing 1–2 mL of alcohol) by the reaction of 4-chloro-2-nitro aniline (**1**)/amino acids (**1'**) and aromatic aldehydes (**2**)/1*H* indole-2,3-diones (**2'**), respectively, with thiosemicarbazide (**3**) yielding triazole

(**4**)/spiro indole-triazole (**5**) derivatives in high yields and shorter reaction displaying excellent fluorescent property (Scheme 1).

One of the tools used to combine economic aspect of new reactions with environmental aspects is the multicomponent reaction strategy. Compound **4** was synthesized by the one-pot multicomponent reaction of **1**, **2**, and **3** in the presence of lemon juice as a natural acidic catalyst in aqueous medium. There are few reports [49, 50] of synthesis of heterocyclic compounds using lemon juice. For the present work, we have used extract of *Citrus limonum* species of lemon as natural catalyst for the synthesis of triazole derivatives. The main ingredients of lemon juice are moisture (85%), carbohydrates (11.2%), citric acid (5–7%), protein (1%), vitamin-C (0.5%), fat (0.9%), minerals (0.3%), fibers (1.6%), and some other organic acids. As lemon juice is acidic in nature (pH $\approx$ 2–3) and percentage of citric acid (5–7%) is more than other acids, it works as acid catalyst [49] for synthesis of triazole derivatives. Using this methodology these reactions were completed in shorter reaction times (1–2 hrs) with yields of the product ranging from 78 to 83%. To our satisfaction, we found that the use of 2 mL of lemon juice resulted in quantitative yield of the corresponding triazole derivatives (**4**) within 1 to 2 hrs.

Mechanism of formation of compound **4** involves acid-catalyzed nucleophilic attack of 4-chloro-2-nitro aniline [**1**] on carbonyl carbon [7] forming arylimino derivatives preferentially [11]. The nucleophilic attack of the amino electrons of thiosemicarbazide at the electrophilic benzyldiene carbon [12] accompanied by the migration of a hydrogen atom forms an intermediate thiol derivative [13] which on cyclisation and desulfurization with the loss of H_2S gives the suggested triazole derivatives (**4**) (Scheme 2).

On the other hand, synthesis of spiro indole triazole (**5**) was carried out in the absence of lemon juice by the reaction

SCHEME 2: Plausible mechanism of formation of compound 4.

SCHEME 3: Plausible mechanism of formation of compound 5.

of **1'**, **2'**, and **3** in the presence of water containing small amount of alcohol as a solvent. The progress of reaction was monitored by TLC. After completion of reaction, mixture was cooled to room temperature and poured on to crushed ice; the product formed was filtered and recrystallized from ethanol.

Formation of spiro indole-triazoles (**5**) (reported by us) [31] took place in the absence of natural acid, formation of which is confirmed by spectral analyses.

The third carbonyl group of isatin being more electrophilic forms 3-aryl imino derivatives preferentially [**14**]. The formation of final compound **5** involves the nucleophilic attack of thiosemicarbazide at the electrophilic indolyl carbon [**14**] accompanied by the migration of hydrogen atom to form an intermediate thiol derivative [**15**]. This is followed by cyclization and desulphurization with the loss of hydrogen sulphide to give the suggested spiro compound **5** (Scheme 3).

In summary, it can be stated that the present green synthetic protocol is highly efficient as it avoids the use of hazardous solvents at any stage of the reaction. The scope of the method was further studied by reacting differently substituted 1H-indole-2,3-diones with amino acids and

thiosemicarbazide. The identity of the products (Tables 3 and 4) obtained was confirmed by their IR, ^1H NMR, and ^{13}C NMR spectral data.

3. Fluorescence Study

A fluorescence study was carried out with newly synthesized triazole derivatives (**4a-j**) and (**5a-l**) in order to relate the fluorescence properties to the nature of donating and acceptor groups attached to these moieties. Fluorescence spectra of 5.7×10^{-5} M solutions of compounds were measured; excitation and emission maxima are also reported. Emission spectra of compounds (**4a-j**) and (**5a-p**) were run in DMSO. The resulting triazoles formed by the reaction of 4-Cl, 2- NO_2 aniline/amino acids and aromatic aldehydes/indole-2,3-diones with thiosemicarbazide result in a bathochromic (red) shift of emission maxima (Tables 1 and 2). The combination of 4-chlorophenyl-substituted triazole to 4-chloro-2-nitro aniline in compound **4d** results in the shift of λ_{em} from 326 to 390.98 nm owing to the electron's withdrawing nature of Cl group. Further, combination of imidazole/indole-substituted

TABLE 1: Fluorescence data of compounds (4a–j).

Entry	Molar concentration	4-Cl, 2-NO ₂ aniline (reactants) λ_{em} ·(nm)	Products λ_{em} ·(nm)
4a	5×10^{-5}	326	376.969
4b	6×10^{-5}	326	362.008
4c	6×10^{-5}	326	355.83
4d	5×10^{-5}	326	390.98
4e	6×10^{-5}	326	354.83
4f	6×10^{-5}	326	360.01
4g	6×10^{-5}	326	353.63
4h	6×10^{-5}	326	356.07
4i	6×10^{-5}	326	354.5
4j	6×10^{-5}	326	354.26

TABLE 2: Fluorescence data of compounds (5a–l).

Entry	Molar concentration	1H-indole-2,3-diones (H, 5-Cl, 5-NO ₂) reactants λ_{em} ·(nm)	Products λ_{em} ·(nm)
5a	7×10^{-5}	296	362.008
5b	6×10^{-5}	296	360.108
5c	6×10^{-5}	296	418.053
5e	6×10^{-5}	296	415.915
5f	7×10^{-5}	296	386.943
5g	7×10^{-5}	296	413.066
5h	6×10^{-5}	296	412.116
5j	5×10^{-5}	291	422.090
5k	5×10^{-5}	291	371.982
5l	5×10^{-5}	291	435.864

triazole in **5j** and **5l** to 5-chloro-1 *H* indole-2,3-dione also results in red shift. For amino substituents, the bathochromic shift of the fluorescence as well of the absorption band is due to the large electron releasing ability of the nitrogen in amine group (**5a–k**) (Figures 1, 2, 3, and 4).

4. Materials and Methods

4.1. General. Reagents and solvents were obtained from commercial sources and used without further purification. Melting points were determined on a Toshniwal apparatus. The ¹H NMR and ¹³C NMR spectra of synthesized compounds have been carried out at SAIF, Punjab University, Chandigarh. ¹H NMR spectra were recorded on Bruker Avance II 400 NMR spectrometer using DMSO-*d*₆ and CDCl₃ as solvent and tetramethylsilane (TMS) as internal reference standard. The purity of compounds was checked on thin layers of silica gel in various nonaqueous solvent systems, for example, benzene : ethyl acetate (8 : 2). IR spectra were recorded in KBr on a Perkin Elmer Infrared L1600300 spectrum Two Li-Ta spectrophotometer and fluorescence studies were carried out on RF-5301 PC spectrofluorophotometer, Shimadzu at FET, MITS, Laxmangarh, Sikar, Rajasthan, India.

FIGURE 1: Fluorescence spectra of compounds (4a–e).

4.2. General Procedure for the Synthesis of Compounds (4a–j). An equimolar mixture of substituted aromatic aldehyde (0.01 mol), 4-chloro-2-nitro aniline (0.01 mol), and methyl phenyl thiosemicarbazide in water (15 mL containing 1–2 mL of ethanol) in the presence of lemon juice (2 mL) was mixed in round bottom flask and the mixture was refluxed for the time needed to complete the reaction (as monitored by TLC). After completion of the reaction, mixture was cooled to room temperature and the solid mass was filtered and recrystallized from ethanol.

4.3. General Procedure for the Synthesis of Compounds (5a–p). An equimolar mixture of substituted 1H-indole-2,3-dione (0.012 mol), substituted amino acids (0.012 mol) and thiosemicarbazide in water (15 mL containing 1–2 mL of ethanol) was mixed in round bottom flask and the mixture was refluxed for the time needed to complete the reaction (as monitored by TLC). The initial syrupy reaction mixture solidifies within 2–3 hours. After completion of the reaction, mixture was cooled to room temperature and the solid mass was poured onto crushed ice, filtered, and recrystallized from ethanol.

5. Antimicrobial Activity

Synthesized compounds **4a–j** and **5a–p** were evaluated for antibacterial and antifungal activity.

5.1. Antibacterial Activity. Synthesized compounds (**4a–j**) were screened for their antibacterial activity against Gram-positive bacteria *Bacillus licheniformis*, *Staphylococcus aureus*,

TABLE 3: Physical characterization data of compounds (4a–j).

Entry	Product	Time (hr.)	Yield (%)	M.P. (°C)	Color
4a		1	82	190	Yellow
4b		2	80	220–222	Pale yellow
4c		1.5	81	140	Orange
4d		1	78	180	Orange
4e		1.5	78	200	Orange
4f		1	80	195	Orange

TABLE 3: Continued.

Entry	Product	Time (hr.)	Yield (%)	M.P. (°C)	Color
4g		1	80	220	Orange
4h		1	81	210	Yellow
4i		1.2	82	240	Yellow
4j		1.5	83	160	Orange

and *Micrococcus luteus* and Gram-negative bacteria *Pseudomonas aeruginosa* and *Escherichia coli* by the agar well diffusion method. 5 mL aliquot of nutrient broth was inoculated with the test organism and incubated at 37°C for 24 hours. Sterile nutrient agar plates were also prepared and holes of 5 mm diameter were cut using a sterile cork borer ensuring proper distribution. The test organisms after 24 hours of incubation were spread onto separate agar plates. The chemical compounds were dissolved in DMSO at a particular concentration or poured into appropriately labelled holes using a pipette in aseptic conditions. A hole containing DMSO served as a control. The plates were left at room temperature for two hours to allow the diffusion of the sample followed by incubation at 37°C for 24 hours in inverted position. The antimicrobial activity was determined

by measuring the diameter of the zone (mm) showing complete inhibition with respect to control (DMSO) and reference compounds streptomycin and erythromycin. It has been observed that all the compounds tested showed good to excellent activity against tested bacteria.

Compound **4g** shows good activity against bacteria *Staphylococcus aureus* at 250 ppm concentration. On the other hand, compound **4j** shows excellent activity against bacteria *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Micrococcus luteus* at 500 ppm concentration. Compound **4b** shows good activity against bacteria *Staphylococcus aureus*, *Micrococcus luteus*, and *Escherichia coli* and compound **4d** also shows good activity against bacteria *Pseudomonas aeruginosa*, *Bacillus licheniformis*, and *Micrococcus luteus* at 500 ppm concentration (Table 5, Figure 5).

TABLE 4: Physical characterization data of compounds (5a–p).

Entry	Product	Time (hr)	Yield (%)	M.P. (°C)	Color
5a		1.5	80	105	Red
5b		1.5	72	98	Brown
5c		2	76	140	Dark brown
5d		2	72	185	Dark brown
5e		1.5	77	170	Orange
5f		1	78	195	Orange

TABLE 4: Continued.

Entry	Product	Time (hr)	Yield (%)	M.P. (°C)	Color
5g		1.5	75	90	Brown
5h		1.5	75	140–142	Red
5i		1.5	71	153	Yellow
5j		2	70	180–182	Orange
5k		1.5	70	220	Red
5l		1.5	69	230	Red
5m		1.5	68	210	Pale yellow

TABLE 4: Continued.

Entry	Product	Time (hr)	Yield (%)	M.P. (°C)	Color
5n		1.5	69	207	Pale yellow
5o		2	70	194	Pale yellow
5p		2	70	185	Pale yellow

TABLE 5: Antibacterial evaluation of the synthesized compounds (4a–j).

Compounds	Zone of inhibition (mm)									
	(250 ppm)					(500 ppm)				
	A	B	C	D	E	A	B	C	D	E
4a	6	8	7	9	9	9	6	10	7	—
4b	7	6	9	8	—	9	9	11	10	11
4c	—	9	9	—	8	4	9	4	—	9
4d	6	—	—	8	—	10	10	—	10	—
4e	8	9	6	9	6	9	4	6	10	3
4f	—	—	9	7	8	9	—	9	9	10
4g	7	8	10	—	7	—	10	—	—	11
4h	7	—	9	9	—	3	—	10	6	—
4i	9	7	—	8	9	—	8	9	—	10
4j	9	9	—	9	—	10	9	11	11	—
DMSO	—	—	—	—	—	—	—	—	—	—
Streptomycin	13	10	14	10	11	10	10	14	14	12
Erythromycin	12	11	—	12	—	12	10	—	11	13

A: *Pseudomonas aeruginosa*, B: *Bacillus licheniformis*, C: *Staphylococcus aureus*, D: *Micrococcus luteus*, E: *Escherichia coli*.
 Bold numbers indicate compounds showing good activity.

FIGURE 2: Fluorescence spectra of compounds (4f-j).

FIGURE 3: Fluorescence spectra of compounds (5a-f).

5.2. Antifungal Activity. Antifungal activity was performed by cup plate method at concentration 500 ppm and 250 ppm against *Aspergillus niger*, *Penicillium sp. fusarium oxysporum*, *Alternaria brassicicola*, *Chaetomium orium*, and *Lycopodium sp.* by measuring the zone of inhibition in mm. Sabour and dextrose agar were employed as culture medium, by pouring

FIGURE 4: Fluorescence spectra of compounds (5g-k).

FIGURE 5: Antibacterial evaluation of the synthesized compounds (4a-j) at 500 ppm.

the sterile agar into Petri dishes in aseptic conditions. 0.1 mL of each standardized test organism culture was spread onto agar plates. The test compounds (250 and 500 ppm), the standard drug solutions, and the solvent control (DMSO) were placed in the cavity separately. Then the plates were maintained at -4°C for 1 hour to allow the diffusion of solution into the medium. All the fungal plates were incubated at 28°C for 42–72 hrs and the zone of inhibition was measured in mm.

TABLE 6: Antifungal evaluation of the synthesized compounds (**4a–j**).

Compounds	Zone of inhibition (mm)											
	Concentration (250 ppm)						Concentration (500 ppm)					
	A	B	C	D	E	F	A	B	C	D	E	F
4a	7	9	8	8	8	8	8	8	10	10	9	10
4b	6	7	9	—	—	—	—	9	9	10	—	11
4c	—	9	—	5	9	5	—	8	9	—	12	9
4d	5	—	10	—	—	8	9	—	9	—	11	—
4e	—	8	8	—	8	—	7	—	11	—	—	—
4f	7	7	9	9	—	6	—	8	9	11	—	12
4g	6	6	10	8	—	—	9	7	10	9	9	10
4h	—	9	—	—	9	—	8	9	11	—	11	11
4i	8	8	—	—	8	8	—	6	—	—	10	—
4j	4	—	8	8	—	—	9	—	11	8	9	—
DMSO	—	—	—	—	—	—	—	—	—	—	—	—
Streptomycin	11	11	13	12	13	10	11	—	12	13	15	14
Erythromycin	14	13	10	11	12	13	14	10	—	14	14	12

A: *Aspergillus niger*, B: *Penicillium notatum*, C: *Fusarium oxysporum*, D: *Alternaria brassicicola*, E: *Chaetomium orium*, F: *Lycopodium sp.*
 Bold numbers indicate compounds showing good activity.

The antimicrobial activity was determined by measuring the diameter of the zone (mm) showing complete inhibition with respect to control (DMSO) and reference compounds streptomycin and erythromycin.

Compounds **4d** and **4g** show good activity against fungus *Fusarium oxysporum* at 250 ppm due to presence of –Cl and –OH substituents. Compound **4c** shows excellent activity against fungus *Chaetomium orium* and **4f** shows excellent activity against fungus *Alternaria brassicicola* and *Lycopodium sp.* at 500 ppm. Compound **4h** shows excellent activity against fungus *Fusarium oxysporum*, *Chaetomium orium*, and *Lycopodium sp.* at 500 ppm. Compound **4a** shows good activity against fungus *Fusarium oxyforum*, *Alternaria brassicicola*, and *Lycopodium sp.* at 500 ppm concentration due to the presence of –OH substituent (Table 6, Figure 6).

5.3. Antibacterial Activity. Compound **5j** shows good activity against bacteria *Pseudomonas aeruginosa* and **5k** shows good activity against bacteria *Staphylococcus aureus*, respectively at 250 ppm concentration. Compound **5m** shows excellent activity against bacteria *Staphylococcus aureus* at 250 ppm concentration due to presence of –NO₂ substituent. On the other hand, compounds **5b**, **5g**, and **5n** show excellent activity against bacteria *Escherichia coli* at 500 ppm concentration (Table 7, Figure 7).

5.4. Antifungal Activity. Compound **5d** shows good activity against *Fusarium oxysporum* at 250 ppm concentration. Compounds **5b**, **5h**, and **5m** show good activity against *Lycopodium sp.* at 500 ppm concentration. Compounds **5d** and **5h** show good activity against *Chaetomium orium* at 500 ppm concentration. Compounds **5f** and **5p** also show good activity against *Alternaria brassicicola* at 500 ppm

FIGURE 6: Antifungal evaluation of the synthesized compounds (**4a–j**) at 500 ppm.

concentration; compounds **5e**, **5h**, and **5j** also show good activity against *Fusarium oxysporum* at 500 ppm concentration (Table 8, Figure 8).

6. Spectroscopic Characterization Data

6.1. Spectroscopic Characterization Data of **4a–j**

4-(5-(p-Tolylamino)-4-(4-chloro-2-nitrophenyl)-3,4-dihydro-2H-1,2,4-triazol-3-yl)phenol (**4a**). m.p. 190°C; IR (KBr): 3476,

TABLE 7: Antibacterial evaluation of the synthesized compounds (5a–p).

Compounds	Zone of inhibition (mm)									
	(250 ppm)					(500 ppm)				
	A	B	C	D	E	A	B	C	D	E
5a	8	8	7	9	9	9	6	10	7	—
5b	6	6	9	8	—	—	9	11	10	11
5c	9	9	9	—	8	4	9	4	—	9
5d	—	—	—	8	—	10	10	—	10	4
5e	8	9	6	9	6	—	4	6	10	3
5f	7	—	9	7	8	9	—	9	9	10
5g	—	8	10	—	7	—	10	—	—	11
5h	7	—	9	9	—	3	—	10	6	5
5i	9	7	—	8	9	—	8	9	—	10
5j	11	9	—	9	—	10	9	11	11	—
5k	9	—	11	—	8	8	8	12	2	10
5l	9	7	—	9	9	—	9	—	10	10
5m	—	—	12	8	—	9	—	11	9	—
5n	9	8	8	7	9	—	—	—	9	11
5o	10	8	10	9	7	8	8	12	4	9
5p	9	7	9	6	—	9	9	11	8	—
DMSO	—	—	—	—	—	—	—	—	—	—
Streptomycin	13	10	14	10	11	10	—	14	14	12
Erythromycin	12	11	—	12	—	12	10	—	11	13

A: *Pseudomonas aeruginosa*, B: *Bacillus licheniformis*, C: *Staphylococcus aureus*, D: *Micrococcus luteus*, E: *Escherichia coli*.
 Bold numbers indicate compounds showing good activity.

FIGURE 7: Antibacterial evaluation of the synthesized compounds 5a–p at 500 ppm.

3355, 3169, 2980, 1604, 1580, 1369, 722, 699 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.35 (s, 3H, CH_3), 5.0 (s, 1H, OH), 5.04 (s, 1H, CH), 6.34–7.15 (m, 4H, aromatic), 6.46–6.95 (m, 4H, aromatic), 6.69–7.25 (m, 3H, aromatic), 7.01 (s, 1H, N–H),

8.97 (s, 1H, N–H). ^{13}C NMR (400 MHz, DMSO- d_6): 156.92 (C–OH), 154.98 (C=N), 141.48–129.72 (aromatic carbons), 128.08–116.20 (aromatic carbons), 135.82–112.14 (aromatic carbons), 66.92 (C–H), 24.34 (CH_3) ppm. Anal. calcd for $\text{C}_{21}\text{H}_{18}\text{N}_5\text{O}_3\text{Cl}$: C, 59.51; H, 4.28; N, 16.52. Found: C, 59.68; H, 4.29; N, 16.53.

5-(5-(*p*-Tolylamino)-4-(4-chloro-2-nitrophenyl)-3,4-dihydro-2H-1,2,4-triazol-3-yl)-2-methoxyphenol (**4b**). m.p. 220–222°C; IR (KBr): 3472, 3354, 3140, 2960, 1619, 1506, 1368, 1272, 1204, 1045, 701, 648 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.38 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 5.01 (s, 1H, OH), 5.06 (s, 1H, CH), 6.34–6.81 (m, 4H, aromatic), 6.42–6.51 (m, 3H, aromatic), 6.69–7.98 (m, 3H, aromatic), 7.21 (s, 1H, N–H), 8.98 (s, 1H, N–Hs). ^{13}C NMR (400 MHz, DMSO- d_6): 156.55 (C–OH), 154.98 (C=N), 149.16 (COCH_3), 141.48–135.82 (aromatic carbons), 129.72–123.22 (aromatic carbons), 124.12–112.14 (aromatic carbons), 66.92 (C–H), 56.20 (COCH_3), 24.32 (CH_3) ppm. Anal. calcd for $\text{C}_{22}\text{H}_{20}\text{ClN}_5\text{O}_4$: C, 58.22; H, 4.44; N, 15.43. Found: C, 58.05; H, 4.27; N, 15.42.

4-(4-Chloro-2-nitrophenyl)-4,5-dihydro-5-(3,4-dimethylphenyl)-N-*p*-tolyl-1H-1,2,4-triazol-3-amine (**4c**). m.p. 140°C; IR

TABLE 8: Antifungal evaluation of the synthesized compounds (5a–p).

Compounds	Zone of inhibition (mm)											
	Concentration (250 ppm)						Concentration (500 ppm)					
	A	B	C	D	E	F	A	B	C	D	E	F
5a	7	9	8	9	8	8	8	8	10	10	9	10
5b	8	7	9	—	—	—	—	9	9	10	—	11
5c	6	9	—	8	9	5	—	8	9	—	12	9
5d	4	—	10	—	—	8	9	—	9	—	11	—
5e	—	8	8	—	8	—	7	—	11	—	—	—
5f	7	7	9	9	—	6	—	8	9	11	—	12
5g	6	6	10	8	—	—	9	7	10	9	9	10
5h	8	9	—	—	9	—	8	9	11	—	11	11
5i	8	8	—	—	8	8	—	6	—	—	10	—
5j	4	—	8	8	—	—	9	—	11	8	9	—
5k	7	—	9	10	—	—	8	9	—	7	—	—
5l	—	9	—	—	9	6	—	8	10	10	9	—
5m	9	10	9	9	—	6	—	—	9	9	9	11
5n	—	9	8	7	8	8	—	—	9	—	9	9
5o	9	—	—	—	—	7	8	—	—	10	7	10
5p	8	8	9	7	7	7	7	9	9	11	12	9
DMSO	—	—	—	—	—	—	—	—	—	—	—	—
Streptomycin	11	11	13	12	13	10	11	—	12	13	15	14
Erythromycin	14	13	10	11	12	13	14	10	—	14	14	12

A: *Aspergillus niger*, B: *Penicillium notatum*, C: *Fusarium oxysporum*, D: *Alternaria brassicicola*, E: *Chaetomium orium*, F: *Lycopodium sp.*

Bold numbers indicate compounds showing good activity.

FIGURE 8: Antifungal evaluation of the synthesized compounds (5a–p) at 500 ppm.

(KBr): 3442, 3317, 3110, 2980, 1645, 1600, 1510, 1350, 1260, 1091, 745, 660 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.35 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 5.10 (s, 1H, CH), 6.34–7.18 (m, 4H, aromatic), 6.46–6.95 (m, 3H, aromatic),

6.67–7.20 (m, 3H, aromatic) 7.10 (s, 1H, N–H), 9.01 (s, 1H, N–H). ^{13}C NMR (400 MHz, DMSO- d_6): 154.92 (C=N), 149.10–135.86 (aromatic carbons), 129.76–116.22 (aromatic carbons), 124.18–112.12 (aromatic carbons), 66.98 (C–H), 24.34 (CH_3), 18.12 (CH_3), 17.88 (CH_3) ppm. Anal. calcd for $\text{C}_{23}\text{H}_{22}\text{N}_5\text{O}_2\text{Cl}$: C, 63.37; H, 5.09; N, 16.07. Found: C, 63.55; H, 5.10; N, 16.09.

4-(4-Chloro-2-nitrophenyl)-5-(4-chlorophenyl)-4,5-dihydro-*N*-*p*-tolyl-1*H*-1,2,4-triazol-3-amine (4d). m.p. 180°C; IR (KBr): 3440, 3327, 3114, 2981, 1645, 1600, 1511, 1462, 1388, 1291, 1090, 781, 642 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.35 (s, 3H, CH_3), 5.06 (s, 1H, CH), 6.34–7.15 (m, 4H, aromatic), 6.46–6.95 (m, 4H, aromatic), 6.67–7.20 (m, 3H, aromatic) 7.01 (s, 1H, N–H), 8.83 (s, 1H, N–H). ^{13}C NMR (400 MHz, DMSO- d_6): 154.94 (C=N), 149.10–135.88 (aromatic carbons), 129.78–123.22 (aromatic carbons), 116.28–112.18 (aromatic carbons), 66.92 (C–H), 24.38 (CH_3), ppm. Anal. calcd for $\text{C}_{21}\text{H}_{17}\text{N}_5\text{O}_2\text{Cl}_2$: C, 57.03; H, 3.87; N, 15.83. Found: C, 57.21; H, 3.86; N, 15.84.

3-(5-(*p*-Tolylamino)-4-(4-chloro-2-nitrophenyl)-3,4-dihydro-2*H*-1,2,4-triazol-3-yl)phenol (4e). m.p. 200°C; IR (KBr): 3476, 3355, 3169, 2980, 1604, 1580, 1369, 722, 699 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.35 (s, 3H, CH_3), 5.0 (s, 1H, OH), 5.04 (s, 1H, CH), 6.34–7.15 (m, 4H, aromatic), 6.46–6.95 (m, 4H,

aromatic), 6.67–7.20 (m, 3H, aromatic), 7.23 (s, 1H, N–H), 9.03 (s, 1H, N–H). ^{13}C NMR (400 MHz, DMSO- d_6): 156.24 (C–OH), 154.94 (C=N), 145.10–135.86 (aromatic carbons), 129.72–123.28 (aromatic carbons), 124.18–112.12 (aromatic carbons), 66.94 (C–H), 24.32 (CH_3), ppm. Anal.calcd for $\text{C}_{21}\text{H}_{18}\text{ClN}_5\text{O}_3$: C, 59.51; H, 4.28; N, 16.52. Found: C, 59.34; H, 4.27; N, 16.51.

4-(4-Chloro-2-nitrophenyl)-4,5-dihydro-5-(2,4-dimethylphenyl)-N-p-tolyl-1H-1,2,4-triazol-3-amine (**4f**). m.p. 195°C; IR (KBr): 3477, 3330, 3169 2980, 1604, 1600, 1508, 1369, 1091, 722, 699 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.35 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 5.08 (s, 1H, CH), 6.34–7.15 (m, 4H, aromatic), 6.46–6.95 (m, 3H, aromatic), 6.67–7.20 (m, 3H, aromatic), 7.67 (s, 1H, N–H), 8.99 (s, 1H, N–H). ^{13}C NMR (400 MHz, DMSO- d_6): 154.96 (C=N), 140.42–129.74 (aromatic carbons), 135.82–123.22 (aromatic carbons), 124.16–112.16 (aromatic carbons), 66.92 (C–H), 24.36 (CH_3), 24.14 (CH_3), 16.14 (CH_3). ppm Anal.calcd for $\text{C}_{23}\text{H}_{22}\text{N}_5\text{O}_2\text{Cl}$: C, 63.37; H, 5.09; N, 16.07. Found: C, 63.54; H, 5.08; N, 16.06.

2-(5-(p-Tolylamino)-4-(4-chloro-2-nitrophenyl)-3,4-dihydro-2H-1,2,4-triazol-3-yl)phenol (**4g**). m.p. 220°C; IR (KBr): 3476, 3354, 3158, 1630, 1504, 1341, 1203, 723, 699 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.35 (s, 3H, CH_3), 5.01 (s, 1H, OH), 5.04 (s, 1H, CH), 6.34–7.15 (m, 4H, aromatic), 6.46–6.95 (m, 4H, aromatic), 6.67–7.20 (m, 3H, aromatic), 7.0 (s, 1H, N–H), 8.93 (s, 1H, N–H). ^{13}C NMR (400 MHz, DMSO- d_6): 156.24 (C–OH), 154.92 (C=N), 141.42–135.86 (aromatic carbons), 136.32–124.12 (aromatic carbons), 128.02–112.16 (aromatic carbons), 66.94 (C–H), 24.32 (CH_3), ppm Anal.calcd for $\text{C}_{21}\text{H}_{18}\text{N}_5\text{O}_3\text{Cl}$: C, 59.51; H, 4.28; N, 16.52. Found: C, 59.33; H, 4.26; N, 16.50.

4-(4-Chloro-2-nitrophenyl)-4,5-dihydro-5-(3-methoxyphenyl)-N-p-tolyl-1H-1,2,4-triazol-3-amine (**4h**). m.p. 210°C; IR (KBr): 3476, 3356, 2924, 1629, 1562, 1505, 1369, 1341, 1251, 1203, 1158, 723, 700 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.35 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 5.04 (s, 1H, CH), 6.34–7.15 (m, 4H, aromatic), 6.46–6.95 (m, 4H, aromatic), 6.67–7.98 (m, 3H, aromatic), 7.09 (s, 1H, N–H), 9.01 (s, 1H, N–H). ^{13}C NMR (400 MHz, DMSO- d_6): 154.42 (C=N), 149.16 (COCH_3), 145.62–136.32 (aromatic carbons), 137.72–128.08 (aromatic carbons), 124.16–112.12 (aromatic carbons), 66.94 (C–H), 56.24 (COCH_3), 24.34 (CH_3), ppm. Anal.calcd for $\text{C}_{22}\text{H}_{20}\text{N}_5\text{O}_3\text{Cl}$: C, 60.34; H, 4.60; N, 15.99. Found: C, 60.16; H, 4.62; N, 15.97.

4-(4-Chloro-2-nitrophenyl)-4,5-dihydro-5-(4-methoxyphenyl)-N-p-tolyl-1H-1,2,4-triazol-3-amine (**4i**). m.p. 240°C; IR (KBr): 3477, 3352, 2934, 1627, 1564, 1507, 1364, 1345, 1254, 1201, 1150, 727, 700 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.35 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 5.04 (s, 1H, CH), 6.34–7.15 (m, 4H, aromatic), 6.63–6.95 (m, 4H, aromatic), 6.67–7.98 (m, 3H, aromatic), 7.0 (s, 1H, N–H), 8.93 (s, 1H, N–H). ^{13}C NMR (400 MHz, DMSO- d_6): 156.24 (OCH_3), 154.44 (CH_3), 150.14 (COCH_3), 145.64–135.82 (aromatic carbons), 136.34–124.12 (aromatic carbons), 128.02–112.18 (aromatic carbons), 66.98 (C–H), 55.90 (COCH_3), 55.22 (CH_3), 24.32

(CH_3) ppm, Anal.calcd for $\text{C}_{22}\text{H}_{20}\text{N}_5\text{O}_3\text{Cl}$: C, 60.34; H, 4.60; N, 15.98. Found: C, 60.17; H, 4.62; N, 15.96.

4-(4-Chloro-2-nitrophenyl)-4,5-dihydro-5-(3,4-dimethoxyphenyl)-N-p-tolyl-1H-1,2,4-triazol-3-amine (**4j**). m.p. 160°C; IR (KBr): 3476, 3354, 2922, 1627, 1508, 1464, 1339, 1203, 1134, 1044 793, 699 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.35 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 5.04 (s, 1H, CH), 6.34–7.81 (m, 4H, aromatic), 6.46–6.95 (m, 3H, aromatic), 6.67–7.98 (m, 3H, aromatic), 7.0 (s, 1H, N–H), 8.93 (s, 1H, N–H). ^{13}C NMR (400 MHz, DMSO- d_6): 154.96 (C=N), 150.14 ($2\times\text{COCH}_3$), 149.54 (OCH_3), 147.62 (OCH_3), 141.48–129.74 (aromatic carbons), 124.18–120.08 (aromatic carbons), 123.28–112.14 (aromatic carbons), 66.92 (C–H), 56.24 (CH_3), 56.20 ($2\times\text{COCH}_3$), 24.34 (CH_3) ppm Anal.calcd for $\text{C}_{23}\text{H}_{22}\text{N}_5\text{O}_4\text{Cl}$: C, 59.04; H, 4.74; N, 14.97. Found: C, 59.22; H, 4.76; N, 14.95.

6.2. Spectroscopic Characterization Data of 5a-p

2-(5-Amino-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl) propanoic acid (**5a**). m.p. 105°C; IR (KBr): 3419, 3159, 2980, 1700, 1674, 1593, 1465, 1060, 1091 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 1.23 (d, 3H, CH_3), 2.00 (s, 2H, NH_2 of triazole ring), 3.67 (q, 1H, CH), 7.0 (s, 1H, N–H of triazole ring), 6.88–7.52 (m, 4H, aromatic), 8.0 (s, 1H, NH of indole ring), 11.0 (s, 1H, OH). ^{13}C NMR (400 MHz, DMSO- d_6): 174.12 (C=O, acid), 168.24 (C=O, indole), 162.14 (C=N), 141.16–130.74 (aromatic carbons), 76.56 (N–C–NH), 46.22 (CH), 14.64 (CH_3) ppm. Anal.calcd for $\text{C}_{12}\text{H}_{13}\text{N}_5\text{O}_3$: C, 52.36; H, 4.76; N, 25.44. Found: C, 52.53; H, 4.79; N, 25.48.

2-(5-Amino-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-4-(methylsulfanyl) butanoic acid (**5b**). m.p. 98°C; IR (KBr): 3420, 3150, 2982, 1702, 1675, 1590, 1460, 1062, 780, 672 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.00 (s, 2H, NH_2 of triazole ring), 2.01 (q, 2H, CH_2), 2.09 (s, 3H, CH_3), 2.44 (t, 2H, CH_2), 3.49 (t, 1H, CH), 7.1 (s, 1H, N–H of triazole ring), 6.86–7.54 (m, 4H, aromatic), 8.1 (s, 1H, NH of indole ring), 11.1 (s, 1H, OH). ^{13}C NMR (400 MHz, DMSO- d_6): 174.18 (C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.14–122.14 (aromatic carbons), 75.54 (N–C–NH), 51.22 (CH), 30.08 (CH_2), 28.14 (CH_2), 17.64 (CH_3) ppm. Anal.calcd for $\text{C}_{14}\text{H}_{17}\text{N}_5\text{O}_3\text{S}$: C, 50.14; H, 5.11; N, 20.88. Found: C, 50.36; H, 5.14; N, 20.84.

2-(5-Amino-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-(1H-imidazole-4-yl)propanoic acid (**5c**). m.p. 140°C; IR (KBr): 3422, 3152, 2982, 1708, 1675, 1593, 1530, 1420, 1091 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.01 (s, 2H, NH_2 of triazole ring), 2.78 (dd, 1H, CH), 3.88 (t, 1H, CH), 6.80 (s, 1H, CH), 7.0 (s, 1H, N–H of triazole ring), 7.44 (s, 1H, CH), 6.87–7.53 (m, 4H, aromatic), 8.2 (s, 1H, NH of indole ring), 11.0 (s, 1H, OH), 13.4 (s, 1H, NH). ^{13}C NMR (400 MHz, DMSO- d_6): 174.18 (C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.14–119.62 (aromatic carbons), 75.54 (N–C–NH),

45.22 (CH), 27.12 (CH₂) ppm. Anal.calcd for C₁₅H₁₅N₇O₃: C, 52.78; H, 4.43; N, 28.73. Found: C, 52.58; H, 4.45; N, 28.76.

2-(5-Amino-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4)triazol)-4(2H)-yl)-3-(1H-indole-3-yl)propanoic acid (5d). m.p. 185°C; IR (KBr): 3425, 3155, 2984, 1708, 1677, 1597, 1530, 1420, 1094 cm⁻¹; ¹H NMR (δ ppm DMSO-d₆): 2.02 (s, 2H, NH₂ of triazole ring), 2.65 (dd, 2H, CH₂), 3.88 (t, 1H, CH), 7.1 (s, 1H, N-H of triazole ring), 6.80 (s, 1H, CH), 6.88–7.52 (m, 4H, aromatic), 7.18–7.20 (m, 4H, aromatic), 8.3 (s, 1H, NH of indole ring), 10.1 (s, 1H, NH), 11.1 (s, 1H, OH). ¹³C NMR (400 MHz, DMSO-d₆): 174.18 (C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.14–122.14 (aromatic carbons), 75.54 (N–C–NH), 45.32 (CH), 34.22 (CH₂) ppm. Anal.calcd for C₂₀H₁₈N₆O₃: C, 61.63; H, 4.65; N, 21.53. Found: C, 61.43; H, 4.68; N, 21.55.

2-(5-Amino-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-methylpentanoic acid (5e). m.p. 170°C; IR (KBr): 3427, 3150, 2980, 1701, 1672, 1592, 1533, 1424, 1094 cm⁻¹; ¹H NMR (δ ppm DMSO-d₆): 0.96 (t, 3H, CH₃), 1.06 (d, 3H, CH₃), 1.29 (m, 2H, CH₂), 2.03 (s, 2H, NH₂ of triazole ring), 2.21 (m, 2H, CH₂), 3.48 (d, 1H, CH), 7.0 (s, 1H, N-H of triazole ring), 6.88–7.52 (m, 4H, aromatic), 8.1 (s, 1H, NH of indole ring), 11.1 (s, 1H, OH). ¹³C NMR (400 MHz, DMSO-d₆): 174.18 (C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.14–120.12 (aromatic carbons), 75.54 (N–C–NH), 55.22 (CH), 33.22 (CH), 25.4 (CH₂), 15.3 (CH₃), 11.14 (CH₃) ppm. Anal.calcd for C₁₅H₁₉N₅O₃: C, 56.77; H, 6.03; N, 22.07. Found: C, 56.57; H, 6.06; N, 22.08.

2-(5-Amino-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-methylbutanoic acid (5f). m.p. 195°C; IR (KBr): 3433, 3155, 2988, 1709, 1678, 1595, 1533, 1427, 1094 cm⁻¹; ¹H NMR (δ ppm DMSO-d₆): 1.01 (d, 3H, CH₃), 1.03 (d, 3H, CH₃), 2.1 (s, 2H, NH₂ of triazole ring), 2.39 (m, 1H, CH), 3.49 (d, 1H, CH), 7.1 (s, 1H, N-H of triazole ring), 6.87–7.54 (m, 4H, aromatic), 8.2 (s, 1H, NH of indole ring), 11.2 (s, 1H, OH). ¹³C NMR (400 MHz, DMSO-d₆): 174.12 (C=O, acid), 168.24 (C=O, indole), 162.16 (C=N), 142.12–120.16 (aromatic carbons), 75.58 (N–C–NH), 58.28 (CH), 27.14 (CH₂), 17.14 (CH₃), 17.12 (CH₃) ppm. Anal.calcd for C₁₄H₁₇N₅O₃: C, 55.44; H, 5.65; N, 23.09. Found: C, 55.62; H, 5.68; N, 23.07.

2-(5-Amino-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-hydroxypropanoic acid (5g). m.p. 90°C; IR (KBr): 3480, 3433, 3151, 2986, 1702, 1673, 1595, 1531, 1422, 1091 cm⁻¹; ¹H NMR (δ ppm DMSO-d₆): 2.0 (s, 1H, OH), 2.2 (s, 2H, NH₂ of triazole ring), 3.5 (t, 1H, CH), 3.76 (dd, 2H, CH₂), 7.0 (s, 1H, N-H of triazole ring), 6.89–7.52 (m, 4H, aromatic), 8.1 (s, 1H, NH of indole ring), 11.1 (s, 1H, OH). ¹³C NMR (400 MHz, DMSO-d₆): 174.12 (C=O, acid), 168.22 (C=O, indole), 162.16 (C=N), 142.16–120.18 (aromatic carbons), 75.54 (N–C–NH), 58.22 (CH₂), 51.22 (CH) ppm. Anal.calcd for C₁₂H₁₃N₅O₄: C, 49.48; H, 4.50; N, 24.04. Found: C, 49.66; H, 4.52; N, 24.07.

2-(5-Amino-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-phenylpropanoic acid (5h). m.p. 140–142°C;

IR (KBr): 3431, 3155, 2988, 1709, 1677, 1592, 1534, 1422, 1091 cm⁻¹; ¹H NMR (δ ppm DMSO-d₆): 2.3 (s, 2H, NH₂ of triazole ring), 2.78 (dd, 2H, CH₂), 3.89 (t, 1H, CH), 7.2 (s, 1H, N-H of triazole ring), 6.88–7.52 (m, 4H, aromatic), 7.08–7.12 (m, 5H, aromatic), 8.0 (s, 1H, NH of indole ring), 11.0 (s, 1H, OH). ¹³C NMR (400 MHz, DMSO-d₆): 174.18 (C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.14–122.14 (aromatic carbons), 75.54 (N–C–NH), 45.32 (CH), 34.22 (CH₂) ppm. Anal.calcd for C₁₈H₁₇N₅O₃: C, 61.53; H, 4.88; N, 19.93. Found: C, 61.33; H, 4.86; N, 19.95.

2-(5-Amino-5-chloro-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-phenylpropanoic acid (5i). m.p. 153°C; IR (KBr): 3433, 3151, 2986, 1702, 1673, 1595, 1531, 1422, 1093 cm⁻¹; ¹H NMR (δ ppm DMSO-d₆): 2.1 (s, 2H, NH₂ of triazole ring), 3.03 (dd, 2H, CH₂), 3.88 (t, 1H, CH), 7.3 (s, 1H, N-H of triazole ring), 7.08–7.21 (m, 5H, aromatic), 7.05–7.46 (m, 3H, aromatic), 8.2 (s, 1H, NH of indole ring), 11.1 (s, 1H, OH). ¹³C NMR (400 MHz, DMSO-d₆): 174.18 (C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.14–120.12 (aromatic carbons), 75.54 (N–C–NH), 45.38 (CH), 34.22 (CH₂) ppm. Anal.calcd for C₁₈H₁₆N₅O₃Cl: C, 56.04; H, 4.18; N, 18.15. Found: C, 56.24; H, 4.21; N, 18.17.

2-(5-Amino-5-chloro-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-(1H-imidazole-4-yl)propanoic acid (5j). m.p. 180–182°C; IR (KBr): 3431, 3155, 2989, 1707, 1676, 1598, 1530, 1428, 1091, 721 cm⁻¹; ¹H NMR (δ ppm DMSO-d₆): 2.0 (s, 2H, NH₂ of triazole ring), 3.04 (dd, 2H, CH₂), 3.89 (t, 1H, CH), 6.80 (d, 1H, CH), 7.1 (s, 1H, N-H of triazole ring), 7.44 (d, 1H, CH), 7.05–7.47 (m, 3H, aromatic), 8.1 (s, 1H, NH of indole ring), 11.1 (s, 1H, OH), 13.4 (t, 1H, NH). ¹³C NMR (400 MHz, DMSO-d₆): 174.18 (C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.14–120.12 (aromatic carbons), 75.54 (N–C–NH), 45.38 (CH), 27.12 (CH₂) ppm. Anal.calcd for C₁₅H₁₄N₇O₃Cl: C, 47.94; H, 3.76; N, 26.09. Found: C, 47.74; H, 3.78; N, 26.12.

2-(5-Amino-5-chloro-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-5-(methylsulfanyl) butanoic acid (5k). m.p. 220°C; IR (KBr): 3434, 3152, 2982, 1701, 1672, 1597, 1532, 1426, 1095, 726 cm⁻¹; ¹H NMR (δ ppm DMSO-d₆): 2.1 (s, 2H, NH₂ of triazole ring), 2.01 (q, 2H, CH₂), 2.08 (s, 3H, CH₃), 2.43 (t, 2H, CH₂), 3.49 (t, 1H, CH), 7.0 (s, 1H, N-H of triazole ring), 7.05–7.46 (m, 3H, aromatic), 8.0 (s, 1H, NH of indole ring), 10.1 (t, 1H, NH), 11.1 (s, 1H, OH). ¹³C NMR (400 MHz, DMSO-d₆): 174.12 (C=O, acid), 168.22 (C=O, indole), 162.18 (C=N), 142.18–120.18 (aromatic carbons), 75.58 (N–C–NH), 51.22 (CH), 27.12 (CH₂), 25.14 (CH₂), 17.14 (CH₃) ppm. Anal.calcd for C₁₅H₁₈N₅O₃SCl: C, 46.93; H, 4.73; N, 18.24. Found: C, 46.73; H, 4.70; N, 18.27.

2-(5-Amino-5-chloro-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-(2,3-dihydro-1H-indole-3-yl)propanoic acid (5l). m.p. 230°C; IR (KBr): 3431, 3150, 2980, 1703, 1670, 1595, 1531, 1424, 1097, 729 cm⁻¹; ¹H NMR (δ ppm DMSO-d₆): 1.93 (t, 2H, CH₂), 2.2 (s, 2H, NH₂ of triazole ring), 3.00 (t, 1H, CH), 3.22 (dd, 2H, CH₂), 3.48 (t, 1H, CH), 7.1 (s, 1H,

N–H of triazole ring), 6.35–6.91 (m, 4H, aromatic), 7.06–7.46 (m, 3H, aromatic), 8.3 (s, 1H, NH of indole ring), 10.1 (s, 1H, NH), 11.1 (s, 1H, OH). ^{13}C NMR (400 MHz, DMSO- d_6): 174.18 (C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.14–120.12 (aromatic carbons), 75.54 (N–C–NH), 49.32 (CH), 32.12 (CH_2) ppm. Anal. calcd for $\text{C}_{20}\text{H}_{19}\text{N}_6\text{O}_3\text{Cl}$: C, 56.28; H, 4.49; N, 19.69. Found: C, 56.48; H, 4.46; N, 19.66.

2-(5-Amino-5-nitro-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-phenylpropanoic acid (5m). m.p. 210°C; IR (KBr): 3433, 3152, 2982, 1701, 1675, 1591, 1532, 1422, 1365, 1092 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.1 (s, 2H, NH_2 of triazole ring), 3.03 (dd, 2H, CH_2), 3.88 (t, 1H, CH), 7.3 (s, 1H, N–H of triazole ring), 7.08–7.21 (m, 5H, aromatic), 7.09–7.46 (m, 3H, aromatic), 8.2 (s, 1H, NH of indole ring), 11.1 (s, 1H, OH). ^{13}C NMR (400 MHz, DMSO- d_6): 174.12 (C=O, acid), 168.24 (C=O, indole), 162.14 (C=N), 142.12–120.10 (aromatic carbons), 75.52 (N–C–NH), 45.34 (CH), 34.28 (CH_2) ppm. Anal. calcd for $\text{C}_{18}\text{H}_{16}\text{N}_6\text{O}_5$: C, 54.54; H, 4.07; N, 21.20. Found: C, 54.37; H, 4.09; N, 21.21.

2-(5-Amino-5-nitro-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-(1H-imidazole-4-yl)propanoic acid (5n). m.p. 207°C; IR (KBr): 3431, 3155, 2986, 1704, 1672, 1594, 1536, 1422, 1366 1092 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 2.0 (s, 2H, NH_2 of triazole ring), 3.04 (dd, 2H, CH_2), 3.89 (t, 1H, CH), 6.80 (d, 1H, CH), 7.1 (s, 1H, N–H of triazole ring), 7.44 (d, 1H, CH), 7.04–7.45 (m, 3H, aromatic), 8.1 (s, 1H, NH of indole ring), 11.3 (s, 1H, OH), 13.4 (t, 1H, NH). ^{13}C NMR (400 MHz, DMSO- d_6): 174.14 (C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.18–120.12 (aromatic carbons), 75.52 (N–C–NH), 45.35 (CH), 27.22 (CH_2) ppm. Anal. calcd for $\text{C}_{15}\text{H}_{14}\text{N}_8\text{O}_5$: C, 46.63; H, 3.65; N, 29.01. Found: C, 46.43; H, 3.67; N, 29.03.

2-(5-Amino-5-nitro-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-5-(methylsulfanyl)butanoic acid (5o). m.p. 194°C; IR (KBr): 3434, 3153, 2984, 1702, 1672, 1599, 1533, 1421, 1362 1097 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 1.80 (q, 2H, CH_2), 2.10 (s, 2H, NH_2 of triazole ring), 2.30 (s, 3H, CH_3), 2.50 (t, 2H, CH_2), 3.49 (t, 1H, CH), 7.1 (s, 1H, N–H of triazole ring), 7.78–7.98 (m, 3H, aromatic), 8.2 (s, 1H, NH of indole ring), 11.1 (s, 1H, OH). ^{13}C NMR (400 MHz, DMSO): 174.18 (C=O, acid), 168.22 (C=O, indole), 162.12 (C=N), 142.14–132.76 (aromatic carbons), 75.54 (N–C–NH), 51.22 (CH), 35.02 (CH_2), 27.14 (CH_2), 25.12 (CH_2), 17.64 (CH_3) ppm. Anal. calcd for $\text{C}_{15}\text{H}_{18}\text{N}_6\text{O}_5\text{S}$: C, 45.68; H, 4.60; N, 21.31. Found: C, 44.40; H, 4.26; N, 22.07.

2-(5-Amino-5-nitro-2-oxo-1, 2-dihydrospiro (indole-3, 3-(1, 2, 4) triazol)-4(2H)-yl)-3-(2,3-dihydro-1H-indole-3-yl)propanoic acid (5p). m.p. 185°C; IR (KBr): 3431, 3152, 2982, 1706, 1678, 1594, 1531, 1429, 1365 1093 cm^{-1} ; ^1H NMR (δ ppm DMSO- d_6): 1.93 (t, 2H, CH_2), 2.2 (s, 2H, NH_2 of triazole ring), 3.00 (t, 1H, CH), 3.47 (dd, 2H, CH_2), 3.60 (t, 1H, CH), 7.1 (s, 1H, N–H of triazole ring), 6.35–6.91 (m, 4H, aromatic), 7.78–7.98 (m, 3H, aromatic), 8.1 (s, 1H, NH of indole ring), 10.1 (s, 1H, NH), 11.1 (s, 1H, OH). ^{13}C NMR (400 MHz, DMSO): 174.18

(C=O, acid), 168.26 (C=O, indole), 162.12 (C=N), 142.14–117.14 (aromatic carbons), 75.54 (N–C–NH), 49.32 (CH), 32.12 (CH_2) ppm. Anal. calcd for $\text{C}_{20}\text{H}_{19}\text{N}_7\text{O}_5$: C, 54.92; H, 4.38; N, 22.42. Found: C, 44.40; H, 4.26; N, 22.07.

7. Conclusion

The use of water as a green solvent offers a convenient, non-toxic, and inexpensive reaction medium for the environmentally economic synthesis of triazole derivatives. This procedure is simpler, economical, milder, and faster, including cleaner reactions, high yields of products, and a simple experimental and work-up procedure, which makes it a useful and attractive process and is also consistent with the green chemistry theme which affords good yields. Synthesized compounds are found to be excellent fluorescent materials and potent fungicidal agents.

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