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Original article

Applications of 2-arylhydrazononitriles in synthesis: Preparation of new indole containing 1,2,3-triazole, pyrazole and pyrazolo[1,5-*a*]pyrimidine derivatives and evaluation of their antimicrobial activities

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ABSTRACT

In this effort, 2-arylhdrazononitriles were used as key synthons for the preparation of wide variety of new, uniquely substituted heterocyclic substances. In addition, the results of biological evaluations demonstrate that members of the group prepared have promising antimicrobial activities against Gram negative bacteria, Gram positive bacteria and Yeast. In the synthetic sequences, 3-(1-methyl-1*H*-indol-3-yl)-3-oxo-2-(phenylhydrazono)propanenitrile **2a** and its 2-methyl derivative **2b** were found to react with hydroxylamine hydrochloride to yield the corresponding indolyl-5-amino-2-phenyl-1,2,3-triazoles **4a**,**b**. These amines react with cyanoacetic acid in presence of acetic anhydride either thermally or under microwave irradiation conditions to yield the corresponding cyanoacetamides **5a**,**b**, which condensed readily with dimethylformamide dimethylacetal to yield the enaminonitriles **6a**,**b**. Whereas heating of **6a**,**b** with hydrazine hydrate affords compound **8**, compound **12** is produced when these reactants are subjected to microwave irradiation. We observed that the aminopyrazole **9** reacts with enaminal **13** to yield **14** and that its reactions with enaminones **15** afford **17**. Finally, compound **5** reacts with cinnamaldehyde to yield the corresponding Schiff's base **18** that does not undergo cyclization to form the pyridine derivative **19**. The activities of all new substances synthesized in this investigation were evaluated against a panel of microbial organisms. The results show that **4a**, **4b**, **5b** and **9b** display strong antimicrobial activities against all of the tested organisms.

1. Introduction

Owing to their interesting biological activities and medicinal properties [1–7], indole derivatives have been targets of investigations by several research groups [8–11]. Also, the 1,2,3-triazole ring system has been the focus of numerous studies owing to its importance in industrially interesting materials, such as dyes, anticorrosive agents, photo stabilizers, photographic materials, and agrochemicals [12]. Although the 1,2,3-triazole structural moiety does not occur in nature, it may display biological activities and there are numerous examples in the literature including anti-HIV [13], anti-Gram positive bacterial [14,15], anti-allergic [16,17], anticonvulsant [18], β-lactamase inhibitory [19], selective β3 adrenergic receptor agonism [20], anti-tuberculosis [21] activities. The anticipated biological properties of interesting aroyltriazolylamines that incorporate the indole moiety has encouraged us to explore their synthesis and elucidate their biological activities. Below, we describe the results of an investigation aimed at the preparation of these substances and an evaluation of their biological properties.

2. Result and discussion

2.1. Synthetic chemistry

We recently described an efficient synthesis of the cyanoacetylindole derivative **1a** that can be easily converted to the corresponding hydrazone **2a** [11], a potentially important synthon in synthetic routes targeted at new aroyl-heteroaromatic substances. In an extension of our previous effort leading to the synthesis of 2-substituted-1,2,3-triazole-5-amines [11], we have utilized hydrazones **2a**,**b** as precursors of new indolyl heteroaromatic substances.

The investigation aimed at this goal began with the reactions of **2a**,**b** with hydroxylamine hydrochloride in the presence of sodium acetate, promoted by heating in DMF solutions for 3 h or using microwave irradiation for 60 s. Under these conditions,

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condensation reactions occurred to produce the 2-aryl-1,2,3-triazole-5-amines **4a**,**b**, as indicated by analysis of their ^{13}C NMR spectra which showed carbonyl carbon at δ 180.34 and 183.35 ppm respectively. It is believed that amidooximes **3** are initially formed in these processes and that they undergo cyclization to generate the corresponding 1,2,3-triazole-5-amines through a pathway that has been described previously [11,22,23]. The formed 1,2,3-triazole-5-amines **4a**,**b** were then reacted with cyanoacetic acid in the presence of acetic anhydride under either thermal or microwave irradiation conditions. These reactions afford cyanoacetamides **5a**,**b** in excellent yields (Scheme 1).

The cyanoacetamides **5a**,**b** react with dimethylformamide dimethylacetal (DMF-DMA) to yield the corresponding enamines **6a**,**b** (Scheme 2). Although these processes have the potential of producing mixtures of the enamines stereoisomers **6** and **7**, the fact that only the *E*-isomers **6** are generated was demonstrated by using NOE experiments that show that the vinyl protons in the enamine moiety are located close to the amide NH. The enamines **6a**,**b** react with hydrazine hydrate in refluxing ethanol to yield the acyclic hydrazine derivatives **8a**,**b** that undergo cyclization to form the corresponding aminopyrazole **9a**,**b** when stirred in refluxing pyridine.

In contrast, under microwave irradiation conditions enamines **6a**,**b** react with hydrazine hydrate to afford the corresponding triazolopyridone derivatives **12a**,**b**. It is believed that upon microwave irradiation the formed acyclic hydrazine derivatives **8a**,**b** tautomerize to produce the hydrazones **11a**,**b** that cyclize to generate **12a**,**b** by way of condensation of their active methine moieties with the internal indolyl carbonyl group. In addition, **12a**,**b** are formed by stirring solutions of **5a**,**b** in refluxing DMF containing anhydrous sodium acetate (Scheme 2).

Pyrimidine rings can be inserted into **9a** by reacting these substances with 3-(dimethylamino)- acrolein **13**. These processes yield the corresponding pyrimidinopyrazole **14**. In a similar manner, reactions of **9a**,**b** with enaminones **15a**–**c** either thermally or under microwave irradiation conditions yield the corresponding pyrazolo[1,5-*a*]pyrimidines **17**(Scheme 3).

A strategy was explored to prepare pyridone–triazoles. Accordingly, condensation of cyanoamides **5a**,**b** with cinnamaldehyde affords dienamides **18a**,**b**. However, when treated under a variety of condition designed to promote cyclization, **18a**,**b** do not react to form **19a**,**b** (Scheme 4).

3. Pharmacology

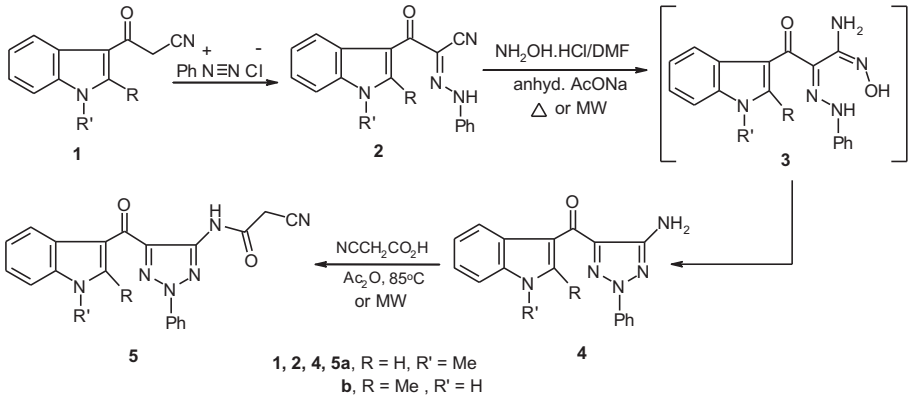
3.1. Methodology

The antimicrobial activities of the compounds prepared in this effort were evaluated using four test organisms, including *Escherichia coli* (Gram negative bacteria), *Bacillus subtilis* and *Staphylococcus aureus* (Gram positive bacteria) and *Candida albicans* (Yeast). An aliquot of 0.1 mL of each bacterial strain was spread on nutrient agar while 0.1 mL of the yeast strain was spread on potato dextrose agar (PDA). An Agar-Well diffusion test was performed in each case, In these tests, 4 mm wells were produced by using a sterile cork borer and each well was then inoculated with 100 μL of each of the key substances in DMSO, resulting in a final concentration of 1 mg mL^{-1}. Nutrient agar plates were incubated at 37 °C for 24 h while the PDA plates were incubated at 25 °C for 48 h. The zones of inhibition around the wells were determined and the averages based on triplicate measurements were recorded. Ampicillin was used as the reference antibacterial agent.

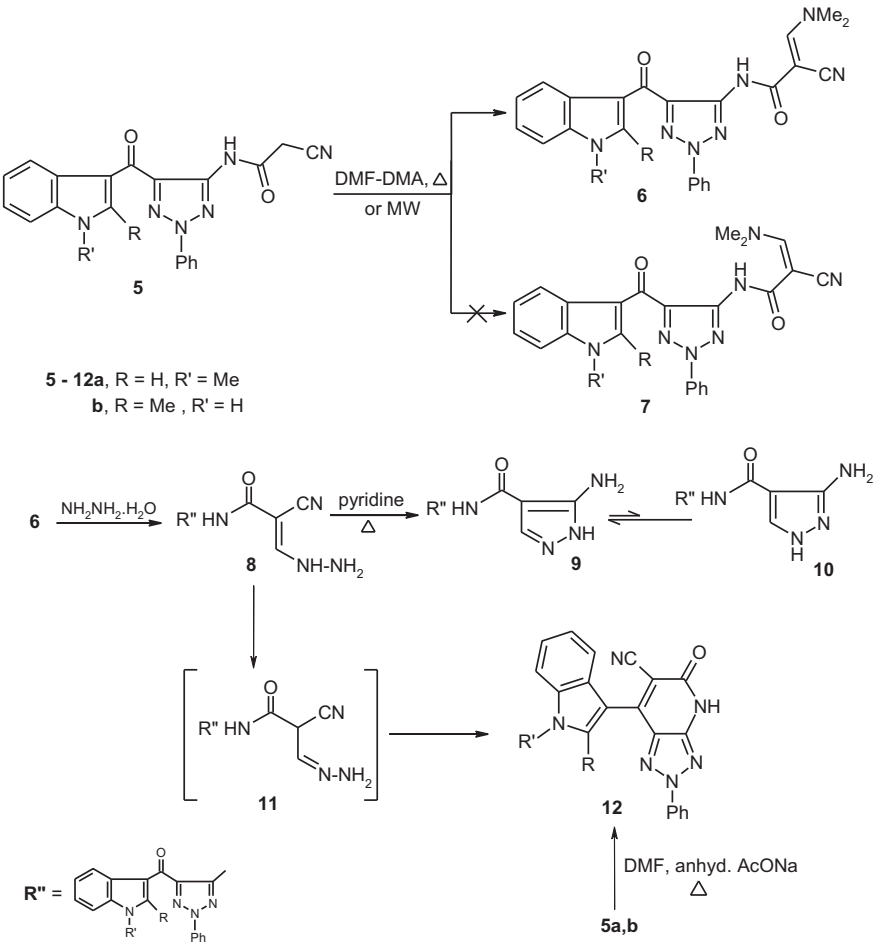
3.2. Antimicrobial evaluation

The results of the antimicrobial activity evaluations, given in Table 1, reveal that substances **4a**, and **4b** exhibit strong activities against the tested organisms while compound **5b** showed activity only towards Gram negative bacteria and one of the Gram positive bacterial strain (*B. subtilis*). Also, **9b** displayed a broad spectrum antibacterial profile only against Gram positive bacteria (*B. subtilis*). In addition, the results displayed in Table 2 indicate that compounds **5a**, **12b**, **17b** and **17c** have moderate growth inhibitory activities against Gram positive bacteria (*B. subtilis*) as revealed by the diameters of their inhibition zones. Among these substances, **12b** and **17b** show moderate growth inhibitory effects on *E. coli* (Gram negative bacteria). Also **17c** has moderate activity against yeast. All of the substances listed in Table 3 exhibit weak antimicrobial activities against the Gram positive bacteria (*B. subtilis*).

The majority of the compounds containing 1,2,3-triazole, pyrazole and pyrazolo[1,5-*a*]- pyrimidine ring systems that incorporate an indole moiety had growth inhibitory activities against the Gram positive bacteria *B. subtilis* but not necessary *S. aureus*. It worth mentioning that the substances **4a**,**b**, possessing a 1,2,3-triazole ring appended to the C3 position of the indole nucleus *via* a ketone linker showed a high antimicrobial activity but the corresponding substances **5a**,**b** in which the triazole is changed to a cyanoacetamide does not. In contrast, attachment of a pyrazole or pyrazolo[1,5-*a*]pyrimidine to the triazole nucleus at position 4 *via* a carboxamide linker, exemplified by compounds **9** and **17**, unfortunately leads to weak to medium antimicrobial activity except **9b** which displayed a broad spectrum antibacterial profile against Gram positive bacteria (*B. subtilis*). Overall, the results showed that four of the heterocycles prepared in this investigation exhibit strong antimicrobial activities with significant inhibition zones (≥10 mm) against at least one of the tested organisms.



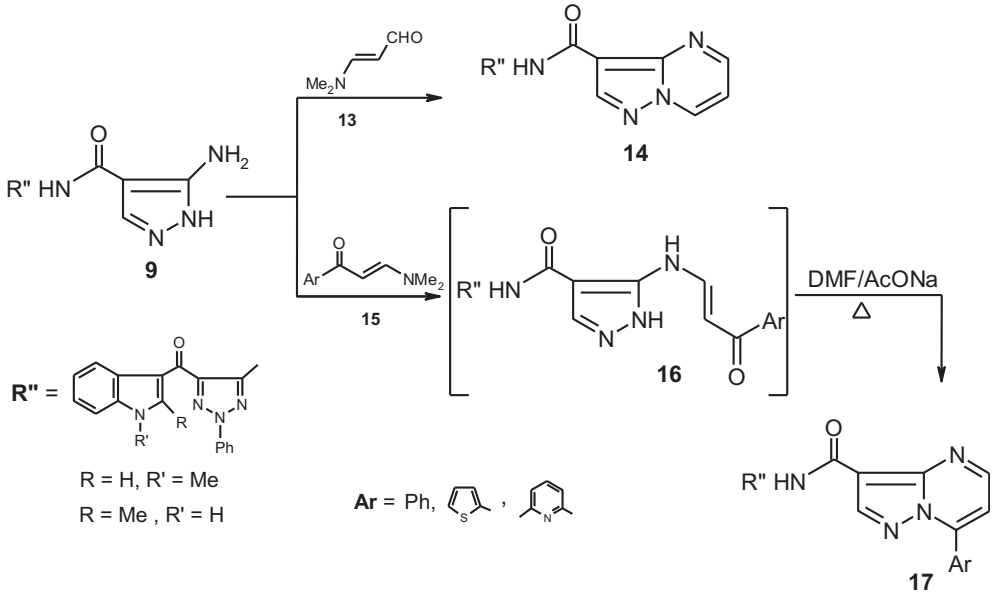
Scheme 1.



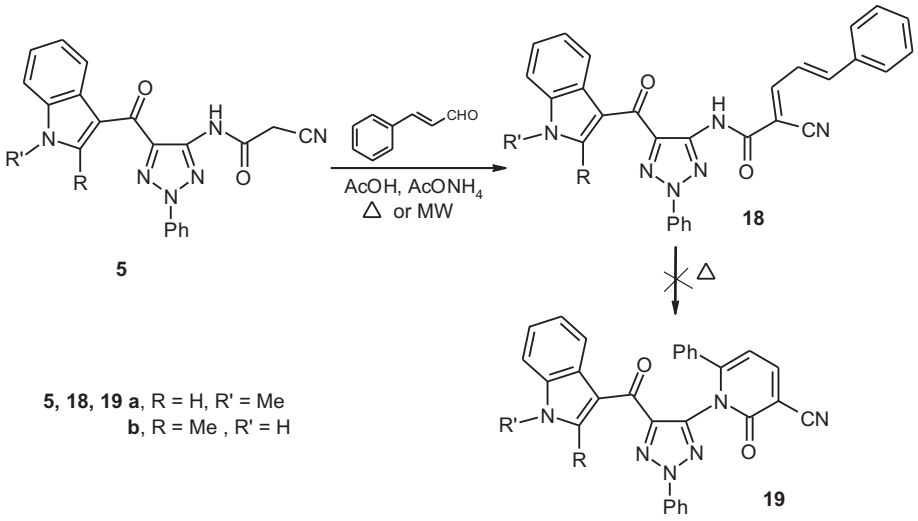
Scheme 2.

4. Conclusion

In this effort, 2-arylhdrazononitriles were used as key synthons for the preparation of a wide variety of new, uniquely substituted heterocyclic substances. In addition, the results of biological evaluations demonstrate that members from the prepared compounds have promising antimicrobial activities against Gram negative bacteria, Gram positive bacteria and Yeast.



Scheme 3.



Scheme 4.

5. Experimental section

5.1. General remarks

All melting points are reported uncorrected. IR spectra were recorded using KBr disks and a Perkin–Elmer System 2000 FT-IR spectrophotometer.^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker DPX 400, 400 MHz NMR spectrometer using $CDCl_3$ or DMSO-d_6 as solvents and TMS as an internal standard. Chemical shifts are reported in ppm. Mass spectra were measured using a high resolution GCMS (DFS) thermo spectrometers with EI (70 EV). Microanalyses were performed on a LECO CHNS-932 Elemental Analyzer. Reactions were conducted under microwave irradiation in heavy-walled Pyrex tubes fitted with PCS caps. Microwave heating was carried out with a single mode cavity Explorer Microwave synthesizer (CEM Corporation, NC, USA). 3-(1-methyl-1*H*-Indol-3-yl)-3-oxopropanenitrile **1a** [24], 3-(2-methyl-1*H*-Indol-3-yl)-3-oxopropanenitrile **1b** [24], 3-(1-methyl-1*H*-indol-3-yl)-3-oxo-2-(phenylhydrazono) propanenitrile **2a** [11] and (5-Amino-2-phenyl-2*H*-1,2,3-triazol-4-yl)(1-methy l-1*H*-indol-3-yl)methanone **4a** [11] were prepared by using literature procedures.

5.2. General procedure for the preparation of ***2a*,*b***

A solution of the aryldiazonium salt (10 mmol) was prepared by adding a solution of sodium nitrite (1.4 g dissolved in 10 mL water) to a stirred solution of the arylamine hydrochloride (10 mmol in 6 mL, 6 M HCl) at 0 °C. The resulting solution was then added to a warm solution of 3-oxoalkanonitriles **1a**,**b** (10 mmol) in ethanol/dioxane mixture (30 mL each) containing sodium acetate trihydrate (4.2 g, 30 mmol). The mixture was stirred at room temperature for 1 h and the resulting solid was collected by filtration, washed with water and ethanol, and crystallized using the indicated solvent.

5.2.1. 3-(1-Methyl-1H-indol-3-yl)-3-oxo-2-(phenylhydrazono) propanenitrile (***2a***)

Recrystallized from a mixture of dioxane/DMF (1:1) as yellow crystals, yield: 2.4 g (80%), mp 199 °C; IR (KBr): ν/cm^{-1} 3225 (NH), 2207 (CN), 1684 (CO); ^{1}H NMR (DMSO-d_6): δ 3.92 (s, 3H, CH_3), 7.14–7.57 (m, 8H, Ar-H), 8.29 (d, J = 7.5 Hz, 1H, Ar-H), 8.40 (s, 1H, indole H-2) and 11.97 ppm (br, 1H, hydrazone NH); ^{13}C NMR (DMSO-d_6): δ 34.45 (CH_3), 111.72, 112.13, 112.79, 115.84 (CN), 117.32, 122.57, 123.37, 124.12, 125.31, 128.06, 130.55, 137.62, 139.71, 143.33 (Ar-C) and 180.46 (CO); MS (EI): m/z (%) 302 (M^+, 45.7), 303 ($M^+ + 1$, 14.6). Anal. Calcd for $C_{18}H_{14}N_4O$ (302.34): C, 71.51; H, 4.67; N, 18.53. Found: C, 71.38; H, 4.58; N, 18.50.

5.2.2. 3-(2-Methyl-1H-indol-3-yl)-3-oxo-2-(phenylhydrazono) propanenitrile (***2b***)

Recrystallized from a mixture of EtOH/dioxane (1:2) as yellow crystals, yield: 2.6 g (85%), mp 223 °C; IR (KBr): ν/cm^{-1} 3371, 3218 (2NH), 2200 (CN), 1667 (CO); ^{1}H NMR (DMSO-d_6): δ 2.56 (s, 3H, CH_3), 7.01–7.07 (m, 2H, Ar-H), 7.14 (t, J = 8.0 Hz, 1H, Ar-H), 7.25 (t, J = 7.8 Hz, 2H, Ar-H), 7.35 (d, J = 8.0 Hz, 2H, Ar-H), 7.41 (d, J = 8.0 Hz, 1H, Ar-H), 7.77 (d, J = 8.0 Hz, 1H, Ar-H), 11.95 (s, 1H, indole NH) and 12.03 ppm (s, 1H, hydrazone NH); ^{13}C NMR (DMSO-d_6): δ 14.60 (CH_3), 111.11, 111.28, 112.10, 114.18, 115.59 (CN), 120.62, 120.86, 121.91, 124.29, 127.17, 129.31, 135.08, 142.24, 143.93 (Ar-C) and 183.08 (CO); MS (EI): m/z (%) 302 (M^+, 14.5), 303 ($M^+ + 1$, 4.8). Anal. Calcd for $C_{18}H_{14}N_4O$ (302.34): C, 71.51; H, 4.67; N, 18.53. Found: C, 71.49; H, 4.73; N, 18.44.

Table 1
Inhibition zone diameters of the tested substances that show strong antimicrobial activities against the tested microorganisms.

Compound no.	Inhibition zone diameter (Nearest mm)			
	E. coli Mean (min-max) SD	*S. aureus* Mean (min-max) SD	*B. subtilis* Mean (min-max) SD	*C. albicans* Mean (min-max) SD
4a	6.7 (4–10)	12.2 (9–17.5)	6 (6–6)	10.7 (8–14)
4b	8.7 (8–10)	12 (10–14)	12 (10–14)	8.7 (6–10)
5b	6.2 (4–8)	0	9.3 (8–10)	0
9b	0	0	11.3 (8–14)	0

Table 2
Inhibition zone diameters of the tested substances that show moderate antimicrobial activities against the tested microorganisms.

Compound no.	Inhibition zone diameter (Nearest mm)			
	E. coli Mean (min-max) SD	*S. aureus* Mean (min-max) SD	*B. subtilis* Mean (min-max) SD	*C. albicans* Mean (min-max) SD
5a	0	0	6 (4–8)	0
12b	4 (4-4)	0	6 (2–10)	0
17b	5 (2–8)	0	8 (6–10)	0
17c	0	0	4 (2–6)	5.7 (3–8)

Table 3
Inhibition zone diameters of the tested substances that show week antimicrobial activities against the tested microorganisms.

Compound no.	Inhibition zone diameter (Nearest mm)			
	E. coli Mean (min-max) SD	*S. aureus* Mean (min-max) SD	*B. subtilis* Mean (min-max) SD	*C. albicans* Mean (min-max) SD
1a	0	0	2 (0–4)	0
1b	0	0	3.3 (2–4)	0
2a	0	0	2.7 (2–4)	0
2b	0	0	1.3 (0–2)	0
6a	0	0	3.3 (2–6)	0
6b	0	0	2.5 (2–3)	0
9a	0	0	2.7 (2–4)	0
12a	0	0	2 (2–2)	0
17a	0	0	3.3 (2–5)	0
17d	0	0	2.7 (2–4)	0
18a	0	0	2.7 (2–4)	0
18b	0	–	3 (1–5)	0
DMSO*	0	0	0	0
Ampicillin**	22 (22–22)	5 (5–5)	1 (1–1)	–

*DMSO (solvent) = Dimethyl sulfoxide.
**Antibacterial drug, (–) not detected.

5.3. General method for the preparation of compounds **4a**,**b**

Independent mixtures of arylhydrazononitriles **2a**,**b** (10 mmol) containing hydroxylamine hydrochloride (1 g, 15 mmol) and anhydrous sodium acetate (2 g) in DMF (20 mL) were stirred at reflux for 2 h or irradiated in a microwave reactor for 60 s at 120 °C. The reaction mixtures were cooled to rt and poured into ice cold water. The formed solids were collected by filtration, washed with water, and crystallized from the indicated solvent.

5.3.1. (5-Amino-2-phenyl-2H-1,2,3-triazol-4-yl)(1-methyl-1H-indol-3-yl)methanone (**4a**)

Recrystallized from a mixture EtOH/DMF (1:1) as yellow crystals, yield: thermally (79%), by microwave (91%); mp: 200–202 °C; IR (KBr): ν/cm^{-1} 3454, 3342 (NH_2), 1608 (CO); ^{1}H NMR (DMSO-d_6): δ 4.01(s, 3H, CH_3), 6.43 (s, 2H, NH_2), 7.27–8.42 (m, 9H, Ar-H) and 8.95 ppm (s, 1H, indole H-2); ^{13}C NMR (DMSO-d_6): δ 33.38 (CH_3), 110.76, 113.07, 118.28, 121.69, 122.36, 123.04, 126.89, 127.41, 129.62, 131.63, 136.93, 138.96, 139.12, 155.67 (Ar and triazole carbons) and 180.34 (CO); MS (EI): *m*/*z* (%) 317 (M^+, 46.8), 318 ($M^+ + 1$, 16.3). Anal. Calcd for $C_{18}H_{15}N_5O$ (317.35): C, 68.13; H, 4.76; N, 22.07. Found: C, 68.25; H, 4.72; N, 21.99.

5.3.2. (5-Amino-2-phenyl-2H-1,2,3-triazol-4-yl)(2-methyl-1H-indol-3-yl)methanone (**4b**)

Recrystallized from a mixture EtOH/H_2O (2:1) as pale yellow crystals, yield: thermally (80%), by microwave (94%); mp: 101 °C; IR (KBr):ν/cm^{-1} 3464, 3330 (NH_2), 3244 (NH), 1630 (CO); ^{1}H NMR (DMSO-d_6): δ 2.66 (s, 3H, CH_3), 6.38 (s, 2H, NH_2), 7.09–7.17 (m, 2H, Ar-H), 7.36 (t, J = 7.6 Hz, 1H, Ar-H), 7.41 (d, J = 8.0 Hz, 1H, Ar-H), 7.52 (t, J = 7.8 Hz, 2H, Ar-H),7.91–7.93 (m, 3H, Ar-H) and 11.94 ppm (s, 1H, indole NH); ^{13}C NMR (DMSO-d_6): δ 14.91 (CH_3), 111.15, 113.08, 117.75, 120.79, 120.85, 121.86, 127.16, 127.31, 129.73, 132.61, 135.00, 139.10, 143.66, 155.60 (Ar and triazole carbons) and 183.35 (CO); MS (EI): *m*/*z* (%) 317 (M^+, 100), 318 ($M^+ + 1$, 29.8). Anal. Calcd for $C_{18}H_{15}N_5O$ (317.35): C, 68.13; H, 4.76; N, 22.07. Found: C, 68.08; H, 4.67; N, 22.15.

5.4. General procedure for the preparation of **5a**,**b**

Independent solutions of cyanoacetic acid (10 mmol) in Ac_2O (10 mL) were heated at 85 °C for 5 min. To each was added either **4a** or **4b**. Each solution was stirred at 85 °C for 30 min Alternatively, solutions of cyanoacetic acid (10 mmol) in Ac_2O (10 mL) were irradiated in a microwave oven at 80 °C for 10 s. Then **4a**,**b** were added and the reaction mixtures were irradiated for further 10 s at the same temperature. All of the reaction mixtures were cooled and poured into cold water. The solid products **5a**,**b** were collected by filtration and crystallized from the indicated solvent.

5.4.1. 2-Cyano-N-[5-(1-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]acetamide (**5a**)

Recrystallized from a mixture EtOH/DMF (3:1) as creamy white crystals, yield: thermally (58%), by microwave (92%), mp 234 °C; IR (KBr): ν/cm^{-1} 3303 (NH), 2252 (CN), 1691, 1601 (2CO); ^{1}H NMR (DMSO-d_6): δ 3.99 (s, 3H, CH_3), 4.16 (s, 2H, CH_2), 7.31–7.38 (m, 2H, Ar-H), 7.52 (t, J = 7.2 Hz, 1H, Ar-H), 7.62–7.67 (m, 3H, Ar-H), 8.17 (d, J = 8.0 Hz, 2H, Ar-H), 8.36 (d, J = 8.0 Hz, 1H, Ar-H), 8.79 (s, 1H, indole H-2) and 10.79 ppm (s, 1H, hydrazone NH); ^{13}C NMR (DMSO-d_6): δ 26.37 (CH_2), 33.45 (CH_3), 110.99, 113.33, 115.59 (CN), 118.97, 121.54, 122.77, 123.41, 126.60, 128.52, 129.83, 137.23, 137.68, 138.72, 140.43, 144.52, 161.35 (Ar-C) and 178.80 ppm (CO); MS (EI): *m*/*z* (%) 384 (M^+, 91.43), 385 ($M^+ + 1$, 25.95). Anal. Calcd. for $C_{21}H_{16}N_6O_2$ (384.40): C, 65.62; H, 4.20; N, 21.86. Found: C, 65.55; H, 4.18; N, 21.92.

5.4.2. 2-Cyano-N-[5-(2-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]acetamide (**5b**)

Recrystallized from a mixture EtOH/DMF (3:1) as creamy white crystals, yield: thermally (61%), by microwave (90%), mp 255 °C; IR (KBr): ν/cm^{-1} 3426, 3332 (2NH), 2256 (CN), 1715, 1601 (2CO); ^{1}H NMR (DMSO-d_6): δ 2.45 (s, 3H, CH_3), 4.03 (s, 2H, CH_2), 7.10–7.20 (m, 2H, Ar-H), 7.43–7.47 (m, 2H, Ar-H) 7.58 (t, J = 8.0 Hz, 2H, Ar-H), 7.77 (d, J = 8.0 Hz, 1H, Ar-H), 7.97 (d, J = 7.6 Hz, 2H, Ar-H), 11.23 (s, 1H, NH) and 12.10 ppm (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.46 (CH_3), 26.00 (CH_2), 111.38, 113.03, 115.48 (CN), 118.31, 120.41, 121.57, 122.30, 127.29, 128.21, 129.93, 135.05, 138.75, 140.53, 142.31, 145.90, 161.52 (Ar-C) and 181.59 ppm (CO); MS (EI): *m*/*z* (%) 384 (M^+, 98.65), 385 ($M^+ + 1$, 30.80). Anal. Calcd. for $C_{21}H_{16}N_6O_2$ (384.40): C, 65.62; H, 4.20; N, 21.86. Found: C, 65.66; H, 4.27; N, 21.79.

5.5. General method for the preparation of compounds **6a**,**b**

Mixtures of **5a**,**b** (3.84 g, 10 mmol), *N*,*N*-dimethylformamide dimethylacetal (DMF-DMA) (1.2 mL, 10 mmol) in DMF (20 mL) were stirred at reflux for 2 h or irradiated in a microwave oven at 120 °C for 60 s. The reaction mixtures were cooled to room temperature and poured into ice cold water containing a few drops from hydrochloric acid. The formed solid products were collected by filtration, washed with water then ethanol and crystallized from the indicated solvent.

5.5.1. (E)-2-Cyano-3-(dimethylamino)-N-[5-(1-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]acrylamide (**6a**)

Recrystallized from a mixture EtOH/DMF (1:1) as buff crystals, yield: thermally (91%), by microwave (98%), mp 240 °C; IR (KBr): ν/cm^{-1} 3438 (NH), 2188 (CN), 1685, 1611 (2CO); ^{1}H NMR (DMSO-d_6): δ 3.27 (s, 3H, CH_3), 3.33 (s, 3H, CH_3), 4.01 (s, 3H, CH_3), 7.30–7.37 (m, 2H, Ar-H), 7.49 (t, J = 7.2 Hz, 1H, Ar-H), 7.60–7.65 (m, 3H, Ar-H), 7.90 (s, 1H, olefinic CH), 8.20 (d, J = 8.0 Hz, 2H, Ar-H), 8.37 (d, J = 7.8 Hz, 1H, Ar-H) 8.97 (s, 1H, indole H-2) and 10.38 ppm (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 33.54(CH_3), 38.40(CH_3), 47.31(CH_3), 69.53(C-2), 111.00, 112.88(CN), 118.90, 119.12, 121.74, 122.81, 123.41, 126.70, 128.28, 129.76, 134.66, 137.11, 138.86, 140.28, 147.21, 157.14, 161.80 (Ar-C and olefinic C) and 179.92 (CO); MS (EI): *m*/*z* (%) 439 (M^+, 38.24%), 440 ($M^+ + 1$, 11.85%). Anal. Calcd for $C_{24}H_{21}N_7O_2$ (439.48): C, 65.59; H, 4.82; N, 22.31. Found: C, 65.71; H, 4.85; N, 22.28.

5.5.2. (E)-2-Cyano-3-(dimethylamino)-N-[5-(2-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]acrylamide (**6b**)

Recrystallized from a mixture EtOH/DMF (1:1) as pale brown crystals, yield: thermally (90%), by microwave (98%), mp 231 °C; IR

(KBr): ν/cm^{-1} 3507, 3323 (2NH), 2189 (CN), 1685, 1610 (2CO); ^{1}H NMR (DMSO-d_6): δ 2.54 (s, 3H, CH_3), 3.21 (s, 3H, CH_3), 3.30 (s, 3H, CH_3), 7.10–7.17 (m, 2H, Ar-H), 7.40–7.46 (m, 2H, Ar-H), 7.58 (t, J = 7.2 Hz, 2H, Ar-H), 7.82–7.85 (m, 2H, olefinic CH and Ar-H), 7.97 (d, J = 7.6 Hz, 2H, Ar-H), 10.12 (s, 1H, NH) and 12.04 ppm (s,1H, indole NH); ^{13}C NMR (DMSO-d_6): δ 14.78(CH_3), 38.23(CH_3), 47.12(CH_3), 69.91(C-2), 111.27, 112.99(CN), 118.18, 118.97, 120.66, 121.39, 122.20, 127.31, 127.95, 129.88, 135.03, 138.95, 139.14, 145.07, 145.61, 156.93, 163.19 (Ar-C and olefinic C) and 182.48 (CO); MS (EI): m/z (%) 439 (M^+, 42.50%), 440 (M^+ + 1, 12.73%). Anal. Calcd for $C_{24}H_{21}N_7O_2$ (439.48): C, 65.59; H, 4.82; N, 22.31. Found: C, 65.56; H, 4.79; N, 22.35.

5.6. General method for the preparation of compounds **8a**,**b**

Solutions of the enaminonitrile **6a**,**b** (10 mmol) and hydrazine hydrate (80%, 0.65 mL) in EtOH (50 mL) were stirred at reflux for 15 min and then cooled to room temperature. The formed solids were separated by filtration then washed with EtOH to give creamy white crystals.

5.6.1. (E)-2-Cyano-3-hydrazinyl-N-[5-(1-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]acrylamide (**8a**)

Yield, 2.9 g (68%), mp 188–190 °C; IR (KBr): ν/cm^{-1} 3365, 3306, 3286, 3257 (NH_2 and 2NH), 2192 (CN), 1682, 1644 (CO). ^{1}H NMR (DMSO-d_6): δ 4.02 (s, 3H, CH_3), 5.35 (br, 2H, NH_2), 7.31–9.02 (m, 11H, Ar-H, olefinic CH and indole H-2), 10.32 (br, 1H, NH) and 10.66 ppm (br, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 33.49 (CH_3), 79.14, 110.96, 112.81 (CN), 118.86, 121.69, 122.77, 123.37, 126.65, 128.24, 129.72, 134.24, 134.70, 137.07, 138.82, 140.24, 147.45, 157.17, 162.34 and 179.91 ppm (Ar-C and CO); MS (EI): m/z (%) 426 (M^+, 24.6), 427 (M^+ + 1, 7.5). Anal. Calcd. for $C_{22}H_{18}N_8O_2$ (426.44): C, 61.97; H, 4.25; N, 26.28; Found: C, 62.04; H, 4.29; N, 26.33.

5.6.2. (E)-2-Cyano-3-hydrazinyl-N-[5-(2-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]acrylamide (**8b**)

Yield, 2.5 g (59%), mp 218–220 °C; IR (KBr): ν/cm^{-1} 3437 (br), 3353, 3222, 3191 (NH_2 and 3NH), 2222 (CN), 1683, 1649 (CO). ^{1}H NMR (DMSO-d_6): δ 2.44 (s, 3H, CH_3), 5.82 (br, 2H, NH_2), 7.07–7.98 (m, 10H, Ar-H, olefinic CH and indole H-2), 10.52 (s, 1H, NH), 11.87 (br, 1H, NH) and 11.99 ppm (s, 1H, NH); MS (EI): m/z (%) 426 (M^+, 12.5), 427 (M^+ + 1, 3.9). Anal. Calcd. for $C_{22}H_{18}N_8O_2$ (426.44): C, 61.97; H, 4.25; N, 26.28; Found: C, 61.86; H, 4.34; N, 26.21.

5.7. General method for the preparation of compounds **9a**,**b**

Solutions of **8a**,**b** (5 mmol) in pyridine (20 mL) were stirred at reflux for 2 h and concentrated in vacuo to give a residues which were triturated with EtOH to afford solids. Separation of the solids by filtration gave a solid that was washed with EtOH and crystallized from EtOH/DMF to give faint pink crystals.

5.7.1. 5-Amino-N-[5-(1-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]-1H-pyrazole-4-carboxamide (**9a**)

Yield, 1.55 g (73%), mp 202 °C; IR (KBr): ν/cm^{-1} 3441, 3324, 3221, 3128 (NH_2 and 2NH), 1669, 1621 (2CO). ^{1}H NMR (DMSO-d_6): δ 3.98 (s, 3H, CH_3), 6.10 (br, 2H, NH_2), 7.28–7.36 (m, 2H, Ar-H), 7.49 (t, J = 7.6 Hz, 1H, Ar-H), 7.59–7.66 (m, 3H, Ar-H), 7.90 (s, 1H, pyrazole H-3), 8.18 (d, J = 8.0 Hz, 2H, Ar-H), 8.36 (d, J = 7.6 Hz, 1H, Ar-H), 8.76 (s, 1H, indole H-2), 10.37 (s, 1H, NH) and 12.01 ppm (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 33.42 (CH_3), 95.85, 110.91, 113.61 (CN), 118.77, 121.73, 122.66, 123.34, 126.67, 128.20, 129.83, 137.21, 137.95, 138.92, 140.29, 145.65, 147.25, 157.48, 161.70 and 179.55 ppm (Ar-C and CO); MS (EI): m/z (%) 426 (M^+, 23.4), 427 (M^+ + 1, 6.5). Anal. Calcd. for $C_{22}H_{18}N_8O_2$ (426.44): C, 61.97; H, 4.25; N, 26.28; Found: C, 61.99; H, 4.19; N, 26.26.

5.7.2. 5-Amino-N-[5-(2-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]-1H-pyrazole-4-carboxamide (**9b**)

Yield, 1.45 g (68%), mp 211 °C; IR (KBr): ν/cm^{-1} 3422 (br), 3312, 3213, 3133 (NH_2 and 3NH), 1660 (CO). ^{1}H NMR (DMSO-d_6): δ 2.45 (s, 3H, CH_3), 5.86 (br, 2H, NH_2), 7.09–7.18 (m, 2H, Ar-H), 7.40–7.45 (m, 2H, Ar-H), 7.58 (t, J = 8.0 Hz, 2H, Ar-H), 7.78 (d, J = 8.0 Hz, 1H, Ar-H), 7.98 (d, J = 8.0 Hz, 2H, Ar-H), 8.05 (s, 1H, pyrazole H-3), 10.54 (s, 1H, NH) 11.86 (s, 1H, NH) and 12.01 ppm (s, 1H, indole NH). ^{13}C NMR (DMSO-d_6): δ 14.59 (CH_3), 95.85, 111.25, 113.19 (CN), 118.02, 118.93, 120.44, 121.38, 122.11, 127.38, 127.80, 129.89, 134.97, 135.79, 138.92, 141.03, 143.46, 145.54, 162.20 and 182.07 ppm (Ar-C and CO); MS (EI): m/z (%) 426 (M^+, 44.0), 427 (M^+ + 1, 12.5). Anal. Calcd. for $C_{22}H_{18}N_8O_2$ (426.44): C, 61.97; H, 4.25; N, 26.28; Found: C, 62.03; H, 4.29; N, 26.34.

5.8. General procedure for the preparation of **12a**,**b**

Method A:

Solution of cyanoacetamides **5a**,**b** (5 mmol) in DMF (20 mL) containing anhydrous sodium acetate (2 g) were stirred at reflux for 3 h, cooled to rt and poured into ice cold water. The formed solids were collected by filtration, washed with water and crystallized from the indicated solvent.

Method B:

Mixture of the enaminonitrile **6a**,**b** (5 mmol) and hydrazine hydrate (80%, 0.65 mL excess) in DMF (10 mL) were irradiated in a microwave oven at 120 °C for 90 s. Then the reaction mixtures were cooled to room temperature and poured into ice cold water containing few drops of HCl. The crude solids which formed were collected by filtration, washed with water, and crystallized from the indicated solvent.

5.8.1. 7-(1-Methyl-1H-indol-3-yl)-5-oxo-2-phenyl-4,5-dihydro-2H-1,2,3-triazolo[4,5-b]pyridine-6-carbonitrile (**12a**)

Recrystallized from a mixture EtOH/DMF (1:3) as yellow crystals, yield, 1.40 g (78%), mp above 300 °C; IR (KBr): ν/cm^{-1} 3443 (NH), 2218 (CN) and 1664 (CO). ^{1}H NMR (DMSO-d_6): δ 3.99 (s, 3H, CH_3), 7.25 (t, J = 7.6 Hz, 1H, Ar-H), 7.34 (t, J = 8.0 Hz, 1H, Ar-H), 7.48 (t, J = 7.6 Hz, 1H, Ar-H), 7.58 (t, J = 8.0 Hz, 2H, Ar-H), 7.64 (d, J = 8.0 Hz, 1H, Ar-H), 7.80 (d, J = 8.0 Hz, 1H, Ar-H), 8.02 (d, J = 7.6 Hz, 2H, Ar-H), 8.35 (s, 1H, indole H-2) and 13.00 ppm (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 33.40 (CH_3), 100.39, 105.85, 110.95, 117.12 (CN), 118.98, 120.90, 121.95, 122.77, 125.00, 128.97, 129.91, 130.65, 135.24, 137.31, 138.81, 145.53, 147.84 and 160.95 ppm (Ar-C and CO); MS (EI): m/z (%) 366 (M^+, 100), 367 (M^+ + 1, 27.8). Anal. Calcd. for $C_{21}H_{14}N_6O$ (366.39): C, 68.84; H, 3.85; N, 22.94; Found: C, 68.78; H, 3.89; N, 23.01.

5.8.2. 7-(2-Methyl-1H-indol-3-yl)-5-oxo-2-phenyl-4,5-dihydro-2H-1,2,3-triazolo[4,5-b]pyridine-6-carbonitrile (**12b**)

Recrystallized from a mixture EtOH/DMF (1:3) as yellow crystals, yield, 1.5 g (82%), mp 292 °C; IR (KBr): ν/cm^{-1} 3422, 3384 (2NH), 2222 (CN) and 1645 (CO). ^{1}H NMR (DMSO-d_6): δ 2.56 (s, 3H, CH_3), 7.09 (t, J = 7.6 Hz, 1H, Ar-H), 7.18 (t, J = 7.6 Hz, 1H, Ar-H), 7.40–7.57 (m, 5H, Ar-H), 7.96 (d, J = 8.0 Hz, 2H, Ar-H), 12.01 (s, 1H, NH) and 13.11 ppm (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 13.91 (CH_3), 104.25, 104.99, 111.26, 116.67 (CN), 118.89, 119.95, 120.06, 121.86, 126.41, 128.92, 129.90, 131.17, 135.65, 138.82, 138.99, 147.07, 147.83 and 160.74 ppm (Ar-C and CO); MS (EI): m/z (%) 366 (M^+, 100), 367 (M^+ + 1, 32.7). Anal. Calcd. for $C_{21}H_{14}N_6O$ (366.39): C, 68.84; H, 3.85; N, 22.94; Found: C, 68.91; H, 3.83; N, 22.87.

*5.9. N-[5-(1-Methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]pyrazolo[1,5-a]- pyrimidine-3-carboxamide (**14**)*

A mixture of **9a** (2.15 g, 5 mmol) and 3-(dimethylamino)acrolein (0.5 g, 5 mmol) in pyridine (10 mL) was refluxed for 48 h or heated in the microwave oven at the maximum power and 120 °C for 2 min. Then, the solvent was removed under reduced pressure and the remaining residue was triturated with MeOH to afford crystals, which were then collected by filtration and recrystallized from DMF as pale brown crystals. Yield: thermally (57%), by microwave (89%), mp 234–236 °C; IR (KBr): ν/cm^{-1} 3420 (NH), 1683, 1615 (2CO); ^{1}H NMR ($CDCl_3$): δ 3.93 (s, 3H, CH_3), 7.09 (t, J = 7.6 Hz, 1H, Ar-H), 7.26–7.50 (m, 6H, Ar-H), 8.19 (d, J = 7.6 Hz, 2H, Ar-H), 8.61–8.73 (m, 2H, Ar-H), 8.80 (s, 1H, Ar-H), 8.99 (s, 1H, indole H-2) and 11.84 ppm (s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 33.88 (CH_3), 105.88, 109.48, 109.75, 114.31, 119.31, 122.87, 123.57, 127.50, 127.94, 129.26, 135.01, 136.27, 137.15, 139.04, 139.46, 145.97, 147.51, 147.86, 151.86, 157.11, 158.85 and 180.68 ppm (Ar-C and CO); MS (EI): m/z (%) 462 (M^+, 75.6), 363 (M^+ + 1, 23.9). Anal. Calcd. for $C_{25}H_{18}N_8O_2$ (462.47): C, 64.93; H, 3.92; N, 24.23; Found: C, 64.87; H, 3.95; N, 24.19.

*5.10. General procedure for the preparation of **17a–d***

Mixtures of **9a**,**b** (5 mmol) and enaminone **15a–c** (5 mmol) in pyridine (20 mL) were stirred at reflux for 48 h or irradiated in a microwave oven at the maximum power and 120 °C for 2 min. The reaction mixtures were cooled to room temperature and poured into ice cold water then acidified with hydrochloric acid (2 N), forming solids that were collected by filtration and washed with water then MeOH and recrystallized from the indicated solvent.

*5.10.1. N-[5-(1-Methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]-7-phenyl pyrazolo [1,5-a]pyrimidine-3-carboxamide (**17a**)*

Recrystallized from a mixture of EtOH/DMF (1:4) as pink crystals. Yield: thermally (63%), by microwave (90%), mp 186–188 °C; IR (KBr): ν/cm^{-1} 3423 (NH), 1685, 1611 (2CO); ^{1}H NMR ($CDCl_3$): δ 3.95 (s, 3H, CH_3), 7.18 (d, J = 4.6 Hz, 1H, H-6), 7.35–7.64 (m, 9H, Ar-H), 8.09–8.16 (m, 2H, Ar-H), 7.22(d, J = 7.6 Hz, 2H, Ar-H), 8.67 (d, J = 7.6 Hz, 1H, Ar-H), 8.75 (s, 1H, pyrazole H-2), 8.86 (s, 1H, indole H-2), 9.04 (d, J = 4.6 Hz, 1H, H-5) and 12.04 ppm (s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 33.76 (CH_3), 105.60, 108.78, 109.59, 114.16, 119.11, 122.67, 122.76, 123.36, 127.39, 127.73, 128.78, 129.10, 129.44, 129.92, 131.65, 134.91, 136.98, 138.91, 139.30, 147.09, 147.23, 147.42, 148.04, 151.47, 159.00 and 180.44 ppm (Ar-C and CO); MS (EI): m/z (%) 538 (M^+, 21.7), 539 (M^++1, 7.8). Anal. Calcd. for $C_{31}H_{22}N_8O_2$ (538.57): C, 69.14; H, 4.12; N, 20.81; Found: C, 69.22; H, 4.05; N, 20.95.

*5.10.2. N-[5-(2-Methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]-7-phenyl pyrazolo [1,5-a]pyrimidine-3-carboxamide (**17b**)*

Recrystallized from a mixture EtOH/DMF (1:3) as yellow crystals. Yield: thermally (55%), by microwave (85%), mp 294 °C; IR (KBr): ν/cm^{-1} 3430, 3232 (2NH), 1658, 1616 (2CO); ^{1}H NMR (DMSO-d_6): δ 2.58 (s, 3H, CH_3), 7.12–7.20 (m, 2H, Ar-H), 7.42–7.49 (m, 2H, Ar-H), 7.55–7.67 (m, 6H, Ar-H), 7.89 (d, J = 7.6 Hz, 1H, Ar-H), 8.05 (d, J = 8.0 Hz, 2H, Ar-H), 8.15 (d, J = 7.6 Hz, 2H, Ar-H) 8.77 (s, 1H, pyrazole H-2), 8.96 (d, J = 4.4 Hz, 1H, H-5), 11.07 (s, 1H, NH) and 12.08 ppm (s,1H, NH). ^{13}C NMR (DMSO-d_6): δ 14.80 (CH_3), 104.01, 109.80, 111.26, 113.04, 118.35, 120.59, 121.39, 122.19, 127.29, 128.09, 128.60, 129.69, 129.82, 129.88, 131.67, 135.03, 138.69, 138.90, 144.21, 145.50, 146.13, 146.95, 147.58, 152.59, 158.48 and 182.09 ppm (Ar-C and CO); MS (EI): m/z (%) 538 (M^+, 18.3), 539 (M^+ + 1, 6.0). Anal. Calcd. for $C_{31}H_{22}N_8O_2$ (538.57): C, 69.14; H, 4.12; N, 20.81; Found: C, 69.12; H, 4.19; N, 20.75.

*5.10.3. N-[5-(1-Methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]-7-(thiophen-2-yl) pyrazolo [1,5-a]pyrimidine-3-carboxamide (**17c**)*

Recrystallized from DMF as yellow crystals, yield: thermally (49%), by microwave (76%), mp 207 °C; IR (KBr): ν/cm^{-1} 3433 (NH), 1682, 1606 (2CO); ^{1}H NMR (DMSO-d_6): δ 4.00 (s, 3H, CH_3), 7.34–7.53 (m, 4H, Ar-H), 7.61–7.68 (m, 3H, Ar-H), 8.05 (d, J = 4.4 Hz, 1H, H-6), 8.19–8.35 (m, 3H, Ar-H), 8.48–8.65 (m, 2H, Ar-H), 8.90 (s, 1H, pyrazole H-2), 8.99 (s, 1H, indole H-2), 9.04 (d, J = 4.4 Hz, 1H, H-5) and 11.71 ppm (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 33.45 (CH_3), 104.39, 105.92, 110.83, 113.07, 118.91, 121.83, 122.63, 123.27, 126.78, 128.10, 128.23, 129.40, 129.70, 133.43, 135.28, 135.96, 137.07, 138.87, 139.95, 140.93, 146.20, 146.40, 146.63, 151.65, 157.99 and 179.39 ppm (Ar-C and CO); MS (EI): m/z (%) 544 (M^+, 11.25), 545 (M^+ + 1, 3.8). Anal. Calcd. for $C_{29}H_{20}N_8O_2S$ (544.60): C, 63.96; H, 3.70; N, 20.58; Found: C, 64.03; H, 3.66; N, 20.50.

*5.10.4. N-[5-(1-Methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]-7-(6-methylpyridin -2-yl)pyrazolo[1,5-a]pyrimidine-3-carboxamide (**17d**)*

Recrystallized from a mixture EtOH/DMF (1:3) as pale brown crystals, yield: thermally (61%), by microwave (88%), mp 260–262 °C; IR (KBr): ν/cm^{-1} 3434 (NH), 1674, 1607 (2CO); ^{1}H NMR (DMSO-d_6): δ 2.63(s, 3H, CH_3), 4.03 (s, 3H, CH_3), 7.32–7.35 (m, 2H, Ar-H), 7.49–7.54 (m, 2H, Ar-H), 7.59–7.68 (m, 3H, Ar-H), 8.01–8.03(m, 2H, Ar-H), 8.25 (d, J = 8.0 Hz, 2H, Ar-H), 8.49 (t, J = 8 Hz, 1H, Ar-H), 8.81–8.85 (m, 2H, Ar-H), 8.98 (s, 1H, indole H-2), 9.16 (d, J = 4.4 Hz, 1H, H-5) and 11.78 ppm (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 24.21 (CH_3), 33.49 (CH_3), 104.53, 109.73, 110.87, 113.06, 118.93, 121.82, 122.67, 123.30, 123.70, 126.03, 126.82, 128.25, 129.73, 135.14, 137.08, 137.35, 138.88, 139.96, 145.11, 145.94, 146.40, 146.52, 146.98, 152.48, 157.91, 158.83 and 179.45 ppm (Ar-C and CO); MS (EI): m/z (%) 553 (M^+, 17.0), 554 (M^+ + 1, 6.5). Anal. Calcd. for $C_{31}H_{23}N_9O_2$ (553.59): C, 67.26; H, 4.19; N, 22.77; Found: C, 67.18; H, 4.23; N, 22.84.

*5.11. General procedure for the preparation of compounds **18a**,**b***

Mixtures of cyanoacetamides **5a**,**b** (1.92 g, 5 mmol) and cinnamaldehyde (0.66 g, 5 mmol) in AcOH (15 mL) containing ammonium acetate (1 g) were stirred at reflux for 2 h or subjected to microwave irradiation at 110 °C for 50 s. The mixtures were cooled to rt and poured into ice cold water. The formed solids were collected by filtration, washed with water then ethanol, and crystallized from a mixture EtOH/DMF (2:1) which gave yellow crystals.

*5.11.1. (2E,4E)-2-Cyano-N-[5-(1-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]-5-phenylpenta-2,4-dienamide (**18a**)*

Yield: thermally (77%), by microwave (88%); mp: 218–220 °C; IR (KBr): ν/cm^{-1} 3432(NH), 2209 (CN), 1693, 1605 (2CO), 1555 (C=C); ^{1}H NMR (DMSO-d_6): δ 3.96 (s, 3H, CH_3), 7.21–7.44 (m, 7H, Ar-H), 7.50 (d, J = 6.6 Hz, 1H, CH=), 7.55–7.60 (m, 4H, Ar-H), 7.69 (t, J = 6.5 Hz, 1H, CH=), 8.16–8.19 (m, 3H, Ar-H), 8.38 (d, J = 6.6 Hz, 1H, CH=), 8.84 (s, 1H, indole H-2), and 10.98 ppm (s,1H, NH). MS (EI): m/z (%) 498 (M^+, 31.5), 499 (M^+ + 1, 10.1). Anal. Calcd. for $C_{30}H_{22}N_6O_2$ (498.55): C, 72.28; H, 4.45; N, 16.86; Found: C, 72.35; H, 4.52; N, 16.88.

*5.11.2. (2E,4E)-2-Cyano-N-[5-(2-methyl-1H-indole-3-carbonyl)-2-phenyl-2H-1,2,3-triazol-4-yl]-5-phenylpenta-2,4-dienamide (**18b**)*

Yield: thermally (82%), by microwave (91%); mp: 268 °C; IR (KBr): ν/cm^{-1} 3395, 3263 (2NH), 2209 (CN), 1677, 1606 (2CO); 1550 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.48 (s, 3H, CH_3), 7.11–7.28 (m, 3H, Ar-H), 7.42–7.56 (m, 6H, Ar-H), 7.60 (t, J = 8.0 Hz, 2H, Ar-H), 7.73–7.79 (m, 3H, Ar-H), 8.01 (d, J = 8.0 Hz, 2H, Ar-H), 8.15 (d, J = 6.8 Hz, 1H, CH=), 11.33 (s, 1H, NH) and 12.10 ppm (s,1H, NH). ^{13}C

NMR ($CDCl_3$): δ 14.63 (CH_3), 106.29, 111.34, 112.95, 114.78 (CN), 118.29, 120.41, 121.52, 122.26, 122.91, 127.25, 128.21, 128.58, 129.20, 129.96, 131.04, 134.73, 135.03, 138.80, 140.79, 143.07, 145.86, 148.65, 153.22, 160.12 and 181.76 ppm (Ar-C and CO); MS (EI): *m*/*z* (%) 498 (M^+, 68.6), 499 ($M^+ + 1$, 21.0). Anal. Calcd. for $C_{30}H_{22}N_6O_2$ (498.55): C, 72.28; H, 4.45; N, 16.86; Found: C,72.22; H, 4.48; N, 16.90.

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