Synthesis and reactions of 3-[3-(dimethylamino)propenoyl]-1,7-diphenyl [1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one

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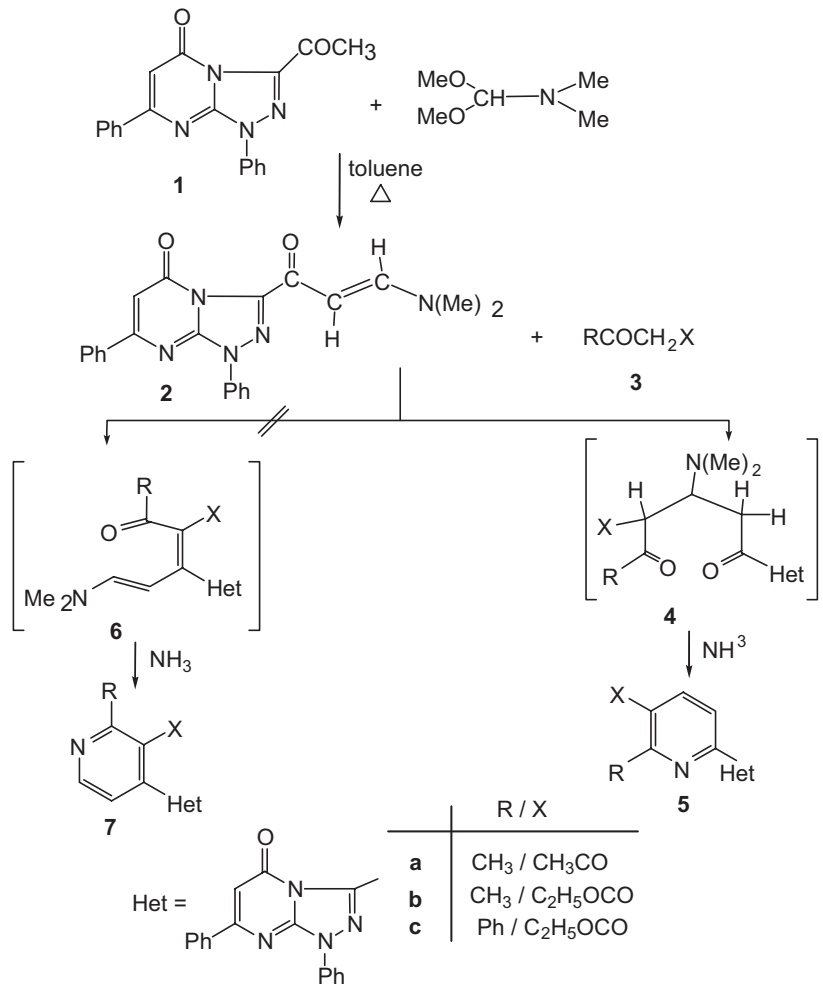
3-Acetyl-1,7-diphenyl[1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (**1**) reacts with *N,N*-dimethylformamide dimethylacetal (DMFDMA) yielding the enaminone **2.** The latter compound reacts with active methylene compounds, hydrazine hydrate, hydroxylamine and some heterocyclic amines to afford trisubstituted pyridine, substituted pyrazole, substituted isoxazole and azolopyrimidines. The antimicrobial activities of the compounds prepared were screened.

Keywords: enaminone, dimethyformamide dimethylacetal, triazolo[4,3-*a*] pyrimidin-5(1*H*)-one, pyridines

The chemistry of enaminones has attracted the interest of many research groups within the last few decades as they have proved to be useful organic synthons.[1,2] Although numerous enaminones have been prepared and their reactions studied, the enaminone **2** namely 3-[3-(dimethylamino) propenoyl]-1,7-diphenyl[1,2,4]triazolo[4,3-*a*]pyrimidin-5 (1*H*)-one has not been reported hitherto. I report here the synthesis of the new enaminone **2** and the results of its chemical reactions with active methylene compounds, hydrazine hydrate, hydroxylamine and some heterocyclic amines. As shown below, the results of such study indicate that this new enaminone **2** is an excellent precursor for synthesis of new functionalised derivatives of 7-phenyl-3-(2-pyridinyl)-[1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one **5** (Scheme 1). The latter derivatives are expected to be useful pharmaceuticals since several 2,3,6-trisubstituted pyridines[3,4] and 1,2,4-triazolo[4,3-*a*]pyrimidinones[5-9] have been reported to exhibit various biological activites.

Results and discussion

The starting enaminone **2** was prepared in this study by reaction of 3-acetyl-1,7-diphenyl[1,2,4]triazolo[4,3-*a*] pyrimidin-5(1*H*)-one **1**[10] with dimethylformamide dimethyl-acetal (DMFDMA) in refluxing toluene. The spectral data (MS, IR, ^{1}H NMR) together with the elemental analysis of the compound **2** are all consistent with the assigned structure



Scheme 1

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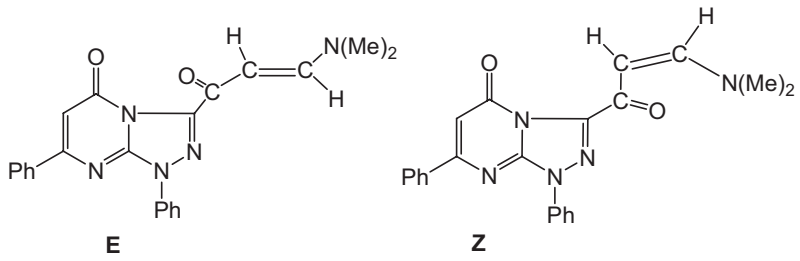


Fig. 1

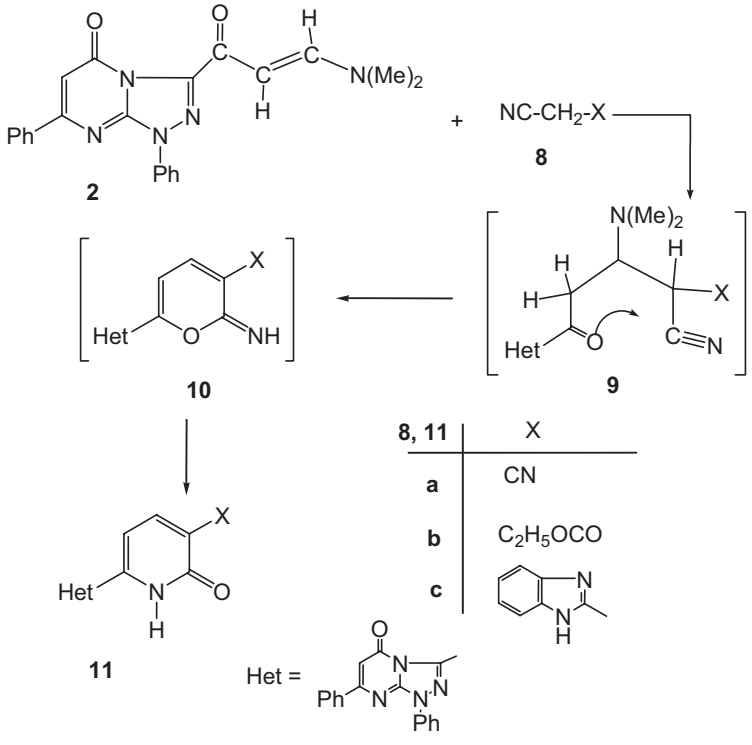
2. Although compound **2** can has two stereoisomeric structures, namely the *Z* and *E* forms (Fig. 1), it seems to exist predominantly in the *E*-form based on ^{1}H NMR data. The ^{1}H NMR spectrum revealed two doublet signals for olefinic protons at δ 5.36 and 8.18 having coupling constant value J = 13 Hz. This value is consistent with the *E*-isomer and not the *Z*-isomer.[11]

Reaction of **2** with acetylacetone **3a** in refluxing acetic acid and in the presence of ammonium acetate gave one isolable product whose mass spectra and IR data are consistent with either structure **5a** or **7a** (Scheme 1). However, structure **5a** was established for the isolated product on the basis of its ^{1}H NMR spectrum. For example, its ^{1}H NMR spectrum revealed two singlet signals at δ 2.69 and 2.88 ppm for the acetyl and methyl protons along with two doublets at δ 8.34 and 8.37 ppm with J = 8.0 Hz. assigned for pyridine H-3 and H-4 respectively. Such coupling value is characteristic for pyridines H-3 and H-4 and much higher than that for H-2 and H-3 (4-6 Hz).[12,13]

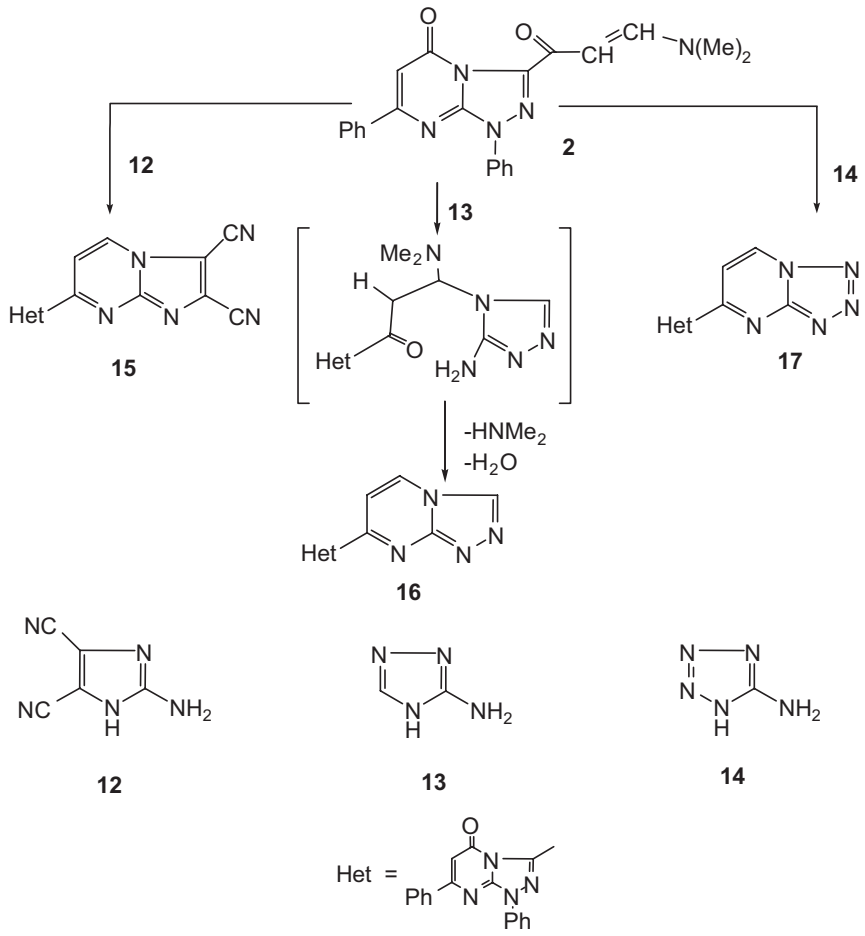
A similar reaction of **2** with each of ethyl acetoacetate **3b** and ethyl benzoyl acetate **3c** in acetic acid and in the presence of ammonium acetate under reflux also afforded the respective products **5b** and **5c**. The ^{1}H NMR spectra of the latter products also revealed in each case two doublet signals with a coupling constant value J = 8.0 Hz which is typical for pyridine H-3 and H-4.[12,13] On the basis of the foregoing data, the other alternating isomeric structure **7** for the isolated products from reaction of **2** with **3a–c** is discarded.

Similarly, the enaminone **2** reacts with active methylene nitriles **8a–c** in refluxing ethanol in the presence of piperidine to yield products that are identified as the pyridinone derivatives **11a–c**, respectively (Sheme 2). The structure assignment of the latter products was based on their spectral (IR, ^{1}H NMR and MS) and elemental analyses data (see Experimental). The formation of **11** may proceed *via* intial Michael addition of the active methylene compounds **8** across the activated double bond yielding the adduct **9** followed by cyclisation and elimination of dimethylamine to give the iminopyran **10** as an intermediate which isomerises to the corresponding **11** *via* the Dimroth type rearrangement.[14]

Reaction of enaminone **2** with heterocyclic amines proved to be excellent synthetic strategy for fused azolopyrimidines. Thus, reacting **2** with 2-aminoimidazole derivative **12,** 3-amino-1,2,4-triazole **13** and 5-aminotetrazole **14** has afforded imidazo[1,2-*a*]pyrimidine **15**. [1,2,4]-triazolo[4,3-*a*] pyrimidine **16** and tetrazolo[1,5-*a*]pyrimidine **17** derivatives, respectively (Scheme 3).The structures of the latter products **15–17** were confirmed by their analytical and spectral (IR, MS, ^{1}H NMR) data (see Experimental). To account for the formation of such products, it is suggested that reaction of **2** with each of **12–14** starts with initial Michael addition of the heterocyclic NH group to the enaminone double



Scheme 2



Scheme 3

bond followed by *in situ* elimination of dimethylamine and condensation of the heterocyclic NH_2 group with the side-chain carbonyl group to give the isolated products **15–17** as end products. This suggested reaction mechanism is similar to literature related reactions.[14-17]

Finally, reaction of the enaminone **2** with some nitrogen nucleophiles were examined. In our hands, the enaminone **2** reacted with hydroxylamine hydrochloride in the presence of sodium acetate in refluxing ethanol to yield the substituted isoxazole **19** rather than **20**. The structure of **19** was established based on the ^{1}H NMR spectrum, which showed a doublet signal at δ 9.15 ppm corresponding to the H-5 of an isoxazole. The alternative product **20** was ruled out as the H-3 proton in **20**, would be expected to resonate at higher field, at around δ 8.3 ppm.[18] Also, compound **2** reacts with each of hydrazine hydrate and guanidine hydrochloride as previously described to yield **18** and **21,** respectively.[19-21]

Antimicrobial activity

All the products were tested for their antimicrobial activities against four fungi species namely *Aspergillus fumigatus* **AF**, *Penicillium italicum* **PI**, *Syncephalastrum racemosum* **SR** and *Candida albican* **CA** as well as four bacteria species

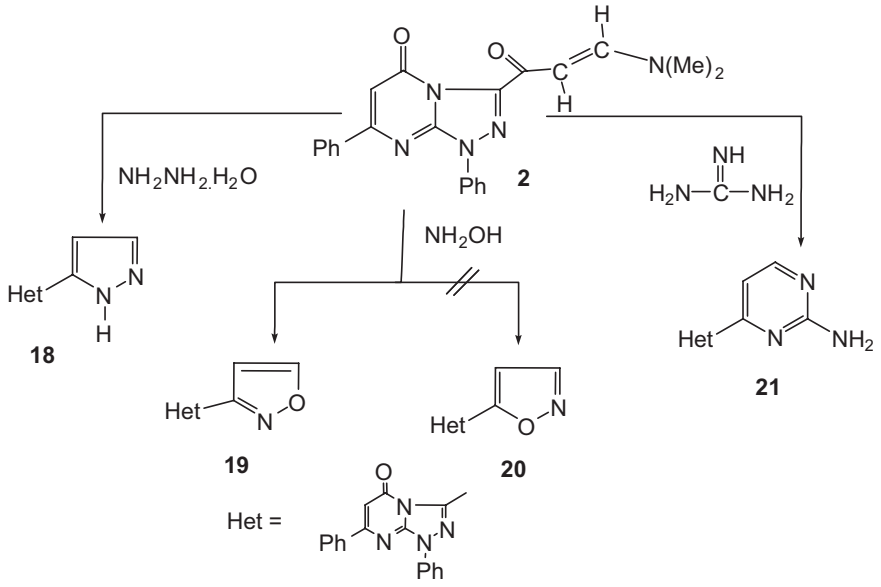
Table 1 Antimicrobial activity of the products

Microorganism/IZC (cm)*								
Compound	**AF**	**PI**	**SR**	**CA**	**SA**	**PA**	**BS**	**EC**
5a	+	+	0	+	0	0	0	0
5b	0	+	0	+	0	0	+	0
5c	0	+ +	0	+	0	0	+	0
11a	+	+	+	0	0	0	+	0
11b	+	+	0	+	0	0	+	0
11c	0	+	0	+	0	0	+	0
15	+	+	0	+	0	0	+	+
18	+	+	+	0	0	+	+	0
19	+ +	+ +	+	0	+ +	+	+ + +	0
21	0	+ +	0	0	0	0	+	0
Te[b]	+ + +	+ + +	+ + +	+ +				
Ch[b]					+ +	+ + +	+ + +	+ +

*IZD, inhibition zone diameter: + + + , inhibition value 1.1–1.5 cm; + + , inhibition value 0.6–1.0 cm, + , inhibition value 0.1–0.5 cm; 0, no inhibition detected.

[a]50 ml solution in DMF, whose concentration of 5 μg/ml was tested.

[b]Te = *Terbinafin* as standard antifungal agent and Ch = *Chloroamphenicol* as the standard antibacterial agent



Scheme 4

namely *Staphylococcus aureus* **SA**, *Pseudomonas aeruginosa* **PA**, *Bacillus subtilis* **BS** and *Escherichia coli* **EC**. The organisms were tested against the activity of solutions of three concentrations namely 1.0, 2.5 and 5 μg/ml of each compound and using inhibition zone diameter in cm as criterion for the antimicrobial activity. Chloroamphenicol as standard antibacterial agent and Terbinafin as standard antifungal agent were used as references to evaluate the potency of the tested compounds under the same conditions. The results obtained using solutions having 5 μg/ml of each compound are summarised in Table 1. Such results showed that the compound **19** exhibited the moderate degree of inhibition against the test fungus species **AF.** The compounds **5c**, **19** and **21** exhibited the moderate degree of inhibition against the test fungus species **PI**. Furthermore, compound **19** inhibited the bacteria species **SA** and **BS**. All other compounds exhibited low or no activity against the microrganisms tested.

Experimental

All melting points were determined on an electrothermal Gallenkamp apparatus and are uncorrected. Solvents were generally distilled and dried by standard literature procedures prior to use. The IR spectra were measured on a Pye-Unicam SP300 instrument in potassium bromide discs. The ^{1}H NMR spectra were recorded on a Varian Mercury VXR-300 spectrometer (300 MHz for ^{1}H NMR) and the chemical shifts were related to that of the solvent DMSO-d6. The mass spectra were recorded on a GCMS-Q1000-EX Shimadzu and GCMS 5988-A HP spectrometers, the ionising voltage was 70 eV. Elemental analyses were carried out by the Microanalytical Centre of Cairo University, Giza, Egypt. 3-acetyl-1,7-diphenyl[1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one **1**[10] was prepared by the literature method.

3-[3-(Dimethylamino)propenoyl]-1,7-diphenyl[1,2,4]triazolo[4,3-a] pyrimidin-5(1H)-one **(2):** A mixture of compound **1** (6.6 g, 20 mmole) and DMFDMA (2.68 g, 20 mmole) in dry toluene (20 ml) was refluxed for 6 h. then left to cool to room temperature. The precipitate was filtered off, washed with ether, dried and recrystallised from ethanol to give orange crystals (6.16 g, 80%), m.p. 212°C. IR: ν_{max} 1685, 1650 cm^{-1}. NMR ($CDCl_3$): δ_H 2.91 (s, 3H, N–CH_3), 3.06 (s, 3H, N–CH_3), 5.36 (d, J = 13 Hz, 2H, =CH), 6.63 (s, 1H, ArH), 7.42–8.17 (m, 10H, ArH), 8.18 (d, J = 13 Hz, 2H, =CH). MS: *m/z* (%) 385 (M^+, 10), 367 (22), 366 (12), 105 (3), 98 (100), 91 (3), 89 (7), 77 (26), 70 (16). Anal. Calcd for $C_{22}H_{19}N_5O_2$ (385.43) C, 68.56; H, 4.97; N, 18.17. Found: C, 68.38; H, 4.69; N, 18.00%.

General procedure for the preparation of 3-(5,6-disubstitutedpyridin-2-yl)-1,7-diphenyl[1,2,4]triazolo[4,3-a] pyrimidin-5(1H)-one **(5a–c)**
To a solution of enaminone **2** (1.93 g, 5 mmole,) and ammonium acetate (0.5 g) in acetic acid (10 ml), the appropriate active methylene compounds **3** (5 mmole) were added. The reaction mixture was heated with stirring under reflux for 3–4 h, and the solvent was evaporated under reduced pressure. The residuel solid formed was filtered and crystallised from ethanol to give products **5a–c**.

3-(6-Acetyl-5-methyl-pyridin-2-yl)-1,7-diphenyl[1,2,4]triazolo [4,3-a]pyrimidin-5(1H)-one **(5a):** White crystals (1.68 g, 80%). m.p. 220°C. IR: ν_{max} 1701, 1681 cm^{-1}. NMR ($CDCl_3$): δ_H 2.69 (s, 3H, CH_3), 2.88 (s, 3H, CH_3), 6.59 (s, 1H, ArH), 7.27–8.15 (m, 10H, ArH), 8.34 (d, J = 8 Hz, 2H, ArH), 8.37 (d, J = 8 Hz, 2H, ArH). MS: *m/z* (%) 422 (M^+ + 1, 13), 421(M^+, 55), 420(47), 236 (14), 129 (35), 109 (25), 105 (12), 91(60), 84(44), 77(29), 57(100), 55(90). Anal. Calcd for $C_{25}H_{19}N_5O_2$ (421. 46) C, 71.25; H, 4.54; N, 16.62. Found: C, 71.03; H, 4.25; N, 16.40%.

3-(6-Ethoxycarbonyl-5-methyl-pyridin-2-yl)-1,7-diphenyl[1,2,4] triazolo[4,3-a]pyrimidin-5(1H)-one **(5b):** White solid (1.65 g, 73%) m.p. 180°C. IR: ν_{max} 1732, 1697 cm^{-1}. NMR ($CDCl_3$): δ_H 1.45 (t, J = 7 Hz, 3H, CH_3), 2.97 (s, 3H, CH_3), 4.44 (q, J = 7 Hz, 2H, CH_2), 6.59 (s, 1H, ArH), 7.27–7.81 and 8.34–8.40 (m, 10H, ArH), 7.78 (d, J = 8 Hz, 2H, ArH), 8.08 (d, J = 8 Hz, 2H, ArH). MS: *m/z* (%) 452 (M^+ + 1, 4), 451 (M^+, 12), 368 (39), 313 (18), 288 (14), 236 (31), 183 (18), 157 (15), 129 (37), 111 (38), 98 (72), 91 (13), 83 (100), 77 (13), 55 (38). Anal. Calcd for $C_{26}H_{21}N_5O_3$ (451.49) C, 69.17; H, 4.69; N, 15.51. Found: C, 69.43; H, 4.43; N, 15.21%.

3-(6-Ethoxycarbonyl-5-phenyl-pyridin-2-yl)-1,7-diphenyl[1,2,4] triazolo[4,3-a] pyrimidin-5(1H)-one **(5c):** Yellow crystals (2.0 g, 79%) m.p. 240°C. IR: ν_{max} 1720, 1685 cm^{-1}. NMR (DMSO-d_6): δ_H 1.08 (t, J = 7 Hz, 3H, CH_3), 4.19 (q, J = 7 Hz, 2H, CH_2), 6.70 (s, 1H, ArH), 7.48–7.70 (m, 15H, ArH), 8.01 (d, J = 8 Hz, 2H, ArH), 8.37 (d, J = 8 Hz, 2H, ArH). MS: *m/z* (%) 515 (M^+ + 2, 25), 514 (M^+ + 1, 90), 513 (M^+, 100), 512 (59), 485 (48), 484 (69), 468 (12), 207 (18), 179 (13), 128 (14), 103 (33), 91 (61), 77 (80). Anal. Calcd for $C_{31}H_{23}N_5O_3$ (513.56) C, 72.50; H, 4.51; N, 13.64. Found: C, 72.24; H, 4.19; N, 13.38%.

3-(5-Cyano-6-oxo-1,6-dihydropyridin-2-yl)-1,7-diphenyl[1,2,4] triazolo[4,3-a]pyrimidin-5(1H)-one **(11a):** To a solution of enaminone **2** (1.93 g, 5 mmole) in ethanol (30 ml) was added malononitrile (0.17 g, 5 mmole) and few drops of piperidine. The reaction mixture was heated on a water bath at 30–40°C for 24 h, then left to cool. The solid so formed was collected by filtration, washed with ethanol and crystallised from dioxane to give red solid (1.42 g, 70%) yield m.p > 300°C. IR: ν_{max} 3386, 2221 1689, 1651 cm^{-1}. NMR ($CDCl_3$): δ_H 6.60 (s, 1H, ArH), 7.27–7.92 (m, 10H, ArH), 8.19 (d, J = 8 Hz, 2H, ArH), 8.29 (d, J = 8 Hz, 2H, ArH), 13.90 (s, 1H, NH). MS: *m/z* (%) 408 (M^+ + 2, 24), 407 (M^+ + 1, 22), 406 (M^+, 44), 288 (72), 287 (88), 129 (64), 117 (20), 103 (62), 91 (78), 77 (100). Anal. Calcd for $C_{23}H_{14}N_6O_2$ (406.41) C, 67.98; H, 3.47; N, 20.68. Found: C, 67.62; H, 3.30; N, 20.45%.

General procedure of preparation of compounds **(11b–c)**
To a solution of enaminone **2** (1.93 g, 5 mmole) and active methylene nitrile compound **8** (0.005 mole) in toluene (30 ml) was added few

drops of piperidine. The reaction mixture was refluxed for 6 h and the solvent was removed under vacuum. The solid so formed was collected by filtration, washed with ethanol and crystallised from ethanol to give compounds **11b–c**.

3-(5-Ethoxycarbonyl-6-oxo-1,6-dihydropyridin-2-yl)-1,7-diphenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one **(11b):** Yellow solid (1.59 g, 70%) m.p. 232°C. IR: ν_{max} 3421, 1716, 1651, 1612 cm^{-1}. NMR ($CDCl_3$): δ_H 1.39 (t, *J* = 7 Hz, 3H, CH_3), 4.34 (q, *J* = 7 Hz, 2H, CH_2), 6.85 (s, 1H, ArH), 7.12 (d, *J* = 9 Hz, 2H, ArH), 7.16–8.32 (m, 10H, ArH), 8.59 (d, *J* = 9 Hz, 2H, ArH), 14.25 (s, 1H, NH). MS: *m/z* (%) 455 (M^+ + 2, 22), 454 (M^+ + 1, 65), 453 (M^+, 88), 406 (12), 380 (100), 353 (12), 287 (11), 145 (13), 129 (28), 120 (17), 116 (13), 103 (18), 91 (27), 77 (66). Anal. Calcd for $C_{25}H_{19}N_5O_4$ (453.46) C, 66.22; H, 4.22; N, 15.44. Found: C, 66.00; H, 4.25; N, 15.24%.

3-(5-(2-benzimidazolyl)-6-oxo-1,6-dihydropyridin-2-yl)-1,7-diphenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one **(11c):** Yellow solid (2.04 g, 82%) m.p. 238°C; IR: ν_{max} 3421, 3058 1691, cm^{-1}. NMR ($CDCl_3$): δ_H 6.63 (s, 1H, ArH), 7.44–8.15 (m, 14H, ArH), 8.16 (d, *J* = 8 Hz, 2H, ArH), 8.23 (d, *J* = 8 Hz, 2H, ArH), 11.0 (s, 1H, NH), 13.82 (s, 1H, NH). MS: *m/z* (%) 497 (M^+, 14), 370 (32), 329 (60), 247 (34), 171 (21), 162 (21), 110 (63), 91 (24), 77 (100). Anal. Calcd for $C_{29}H_{19}N_7O_2$ (497.52) C, 70.01; H, 3.85; N, 19.71. Found: C, 70.10; H, 3.63; N, 19.50%.

General procedure of preparation of compounds **(15–17)**
A mixture of enaminone **2** (1.93 g, 5 mmole) and the appropriate heterocyclic amines **12–14** (6 mmole) in dry toluene (20 ml) was refluxed for 10 h then left to cool to room temperature. The solvent was evaporated under vacuum then the solid so formed was filtered off, washed with ethanol, dried and recrystallised from the appropriated solvent to give products **15–17**.

3-(2,3-Dicyanoimidazo[1,2-a]pyrimidin-7-yl)-1,7-diphenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one **(15)**: Orange solid (1.54 g, 72%) m.p. 222°C (dioxane). IR: ν_{max} 2183, 2144, 1701 cm^{-1}. NMR ($CDCl_3$): δ_H 6.60 (s, 1H, ArH), 7.01–7.32 (m, 10H, ArH), 7.42 (d, *J* = 7 Hz, 2H, ArH), 7.84 (d, *J* = 7 Hz, 2H, ArH). MS: *m/z* (%) 457 (M^+ + 2, 5), 456 (M^+ + 1, 3), 455 (M^+, 100), 454 (42), 352 (16), 287 (32),145 (14), 155 (41), 129 (13), 116 (25), 103 (21), 91 (61), 77 (80). Anal. Calcd for $C_{25}H_{13}N_9O$ (455.44) C, 65.93; H, 2.88; N, 27.68. Found: C, 65.85; H, 3.08; N, 27.46%.

3-([1,2,4]Triazolo[1,5-a]pyrimidine-7-yl)-1,7-diphenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one **(16)**: Yellow crystals (1.50 g, 74%) m.p. 260°C (DMF); IR: ν_{max} 1693 cm^{-1}. NMR ($CDCl_3$): δ_H 6.45 (s, 1H, ArH), 7.27–8.02 (m, 10H, ArH), 7.86 (d, *J* = 9 Hz, 2H, ArH), 8.11 (d, *J* = 9 Hz, 2H, ArH), 8.93 (s, 1H, ArH). MS: *m/z* (%) 408 (M^+ + 2, 18), 407 (M^+ + 1, 65), 406 (M^+, 100), 405 (79), 289 (33), 288 (59), 233 (33), 136 (26), 129 (21), 103 (57), 91 (82), 77 (80). Anal. Calcd for $C_{22}H_{14}N_8O$ (406.41) C, 65.02; H, 3.47; N, 27.57. Found: C, 64.93; H, 3.22; N, 27.34%.

3-[Tetrazolo[1,5-a]pyrimidine-7-yl]-1,7-diphenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one **(17)**: White crystals (1.59 g, 78%) m.p. 204°C; IR: ν_{max} 1689 cm^{-1}. NMR ($CDCl_3$): δ_H 6.63 (s, 1H, ArH), 7.32–7.85 (m, 10H, ArH), 7.91 (d, *J* = 8 Hz, 2H, ArH), 8.10 (d, *J* = 8 Hz, 2H, ArH). MS: *m/z* (%) 408 (M^+ + 1, 4), 407 (M^+, 24), 288 (12), 105 (83), 91 (14), 77 (100). Anal. Calcd for $C_{21}H_{13}N_9O$ (407.40) C, 61.91; H, 3.22; N, 30.94. Found: C, 61.83; H, 3.00; N, 30.63%.

3-[Pyrazol-3-yl]-1,7-diphenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one **(18)**: A mixture of hydrazine hydrate (6 mmole) and enaminone **2** (1.68 g, 5 mmole) in absolute ethanol (30 ml) was refluxed for 2 h, then left to cool to room temperature. The solid formed was filtered off, washed with ethanol, dried and recrystallised from ethanol to give product **18** (1.5 g, 85%) m.p. 170°C. IR: ν_{max} 3116, 1685 cm^{-1}. NMR (DMSO-d_6): δ_H 6.66 (s, 1H, ArH), 7.44–7.53 and 7.64–8.23 (m, 10H, ArH), 7.54 (d, *J* = 8 Hz, 2H, H-pyrazole), 8.25 (d, *J* = 8 Hz, 2H, H-pyrazole), 9.39 (s, 1H, NH). MS: *m/z* 354 (M^+, 41), 353(100), 243(44), 235 (12), 230(41), 181(24), 1733(18), 156(18), 77(49). Anal. Calcd for $C_{20}H_{14}N_6O$ (354.37) C, 67.79; H, 3.98; N, 23.72. Found: C, 67.66; H, 3.86; N, 23.39%.

3-(1,2-Oxazol-3-yl)-1,7-diphenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one **(19)**: A mixture of enaminone **2** (1.68 g, 5 mmole), hydroxylamine hydrochloride (0.3 g, 6 mmole) and sodium acetate anhydrous (7 mmole) in absolute ethanol (30 ml) was refluxed for 5 h, then left to cool. Dilution with water to the reaction mixture gave a solid which was collected by filtration and recrystallised from ethanol/dioxane to yield white crystals (1.46 g, 82%) m.p. > 300°C. IR: ν_{max} 1701 cm^{-1}. NMR (DMSO-d_6): δ_H 6.21 (d, *J* = 8 Hz, 2H, ArH), 6.57 (s, 1H, ArH), 7.41–8.14 (m, 10H, ArH), 9.15 (d, *J* = 8 Hz, 2H, ArH). MS: *m/z* 355 (M^+, 41), 353 (100), 242 (22), 90 (76), 89 (25),77 (88). Anal. Calcd for $C_{20}H_{13}N_5O_2$ (355.36) C, 67.60; H, 3.69; N, 19.71. Found: C, 67.40; H, 3.80; N, 19.53%.

3-(2-Aminopyrimidin-4-yl)-1,7-diphenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one **(21)**: To a mixture of enaminone **2** (1.68 g, 5 mmole) and guanidine hydrochloride (0.5 g, 6 mmole) in absolute ethanol (30 ml), anhydrous potassium carbonate (40 mmole) was added. The reaction mixture was refluxed for 10 hrs., allowed to cool to room temperature and then diluted the solid product was filtered off washed with water, dried and recrystallised from ethanol/dioxane to give orange solid (g, 50%) m.p. 126°C. IR: ν_{max} 3398, 1693 cm^{-1}. NMR (DMSO-d_6): δ_H 6.25 (s, 2H, NH_2), 6.53 (s, 1H, ArH), 7.02–8.11 (m, 10H, ArH), 7.41 (d, *J* = 8 Hz, 2H, ArH), 7.96 (d, *J* = 8 Hz, 2H, ArH). MS: *m/z* 382 (M^+ + 1, 5), 381 (M^+, 5), 380 (40), 287 (24), 134 (52), 105 (17), 94 (100), 91 (32), 77 (84). Anal. Calcd for $C_{21}H_{15}N_7O$ (381.40) C, 66.13; H, 3.96; N, 25.71. Found: C, 66.43; H, 3.89; N, 25.50%.

Antimicrobial assay
Cultures of four fungi species namely Aspergillus fumigatus **AF**, Penicillium italicum **PI**, Syncephalastrum racemosum **SR** and Candida albican **CA** as well as four bacteria species namely Staphylococcus aureus **SA**, Pseudomonas aeruginosa **PA**, Bacillus subtilus **BS** and Escherichia coli **EC** were used to investigate the antimicrobial activity of the compounds **5a–c, 11a–c, 15–18**. The fungicide Terbinafin and the bactericide Chloroamphenicol were used as standard under the same conditions. The antimicrobial activity was assayed biologically using the diffusion plate technique as previously described.[22]

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