Synthesis of Some New Heterocycles Derived from Ethyl 7-Amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate of Biological Importance

Mohamed Salah K. Youssef,* Mohamed S. Abbady, Ragaa A. Ahmed, and Ahmed A. Omar

Department of Chemistry, Faculty of Science, Assiut University, Assiut 71516, Egypt
*E-mail: salah_kamel2000@yahoo.com

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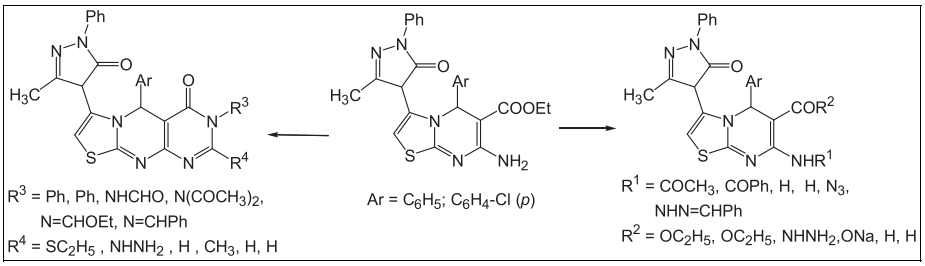

Ethyl 7-amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate was synthesized by the reaction of 4-(2-aminothiazol-4-yl)-3-methyl-5-oxo-1-phenyl-2-pyrazoline with arylidene ethyl cyanoacetate and it transformed to related fused heterocyclic systems *via* reaction with various reagents. The biological activities of these compounds were evaluated.

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INTRODUCTION

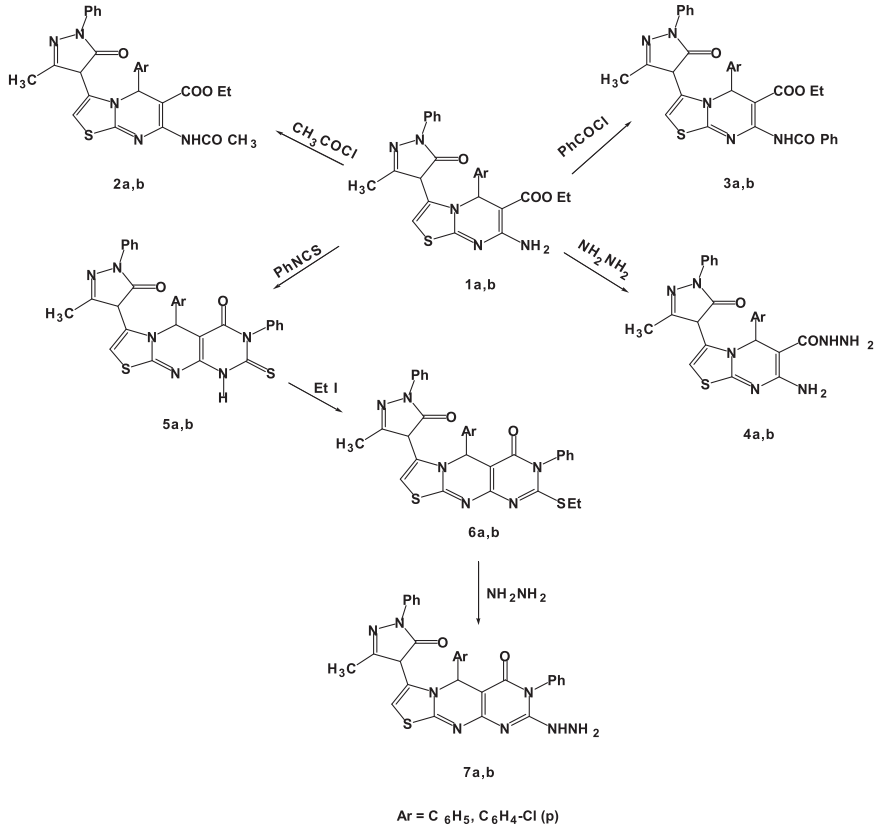
The formation of a new fused heterocyclic ring is an important task for heterocyclic chemistry from various points of view. The reactions of thiazolo[3,2-*a*]pyrimidines have attracted the attention of many chemists and used them in the synthesis of different heterocycles [1–15] possessing biological [10–14] and medicinal activities [15]. These observations in continuation with our general interest in these compounds led us to examine the chemistry of pyrazolinyl thiazolopyrimidine carboxylate to be used as starting material for the synthesis of novel thiazolopyrimidines and thiazolopyrimidopyrimidines bearing pyrazolone moiety, which have biological activities.

RESULTS AND DISCUSSION

This investigation was directed toward the synthesis of novel pyrazolinyl thiazolopyrimidine and pyrazolinyl thiazolopyrimidopyrimidine derivatives. We report herein reactions of ethyl 7-amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate **1a**,**b** to synthesize new compounds containing both pyrazolone, thiazole and pyrimidine moieties, and evaluate their biological activities. Thus reaction of compound **1a**,**b** with acetyl and/or benzoyl chloride gave the corresponding acetyl- or benzoyl derivatives 7-acetylamino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-arylthiazolo [3,2-*a*]pyrimidine **2a**,**b** and/or 7-benzoylamino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-arylthiazolo [3,2-*a*]pyrimidine **3a**,**b**. With hydrazine hydrate, **1a**,**b** gave the corresponding carbohydrazide derivatives 7-amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5*H*-thiazolo [3,2-*a*]pyrimidine-6-carbohydrazide **4a**,**b**. Interaction of **1a**,**b** with phenyl isothiocyanate gave the fused tricyclic compounds 3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-7-phenyl-7,9-dihydro-5*H*-thiazolo[3,2-*a*]pyrimido [4,5-*d*]pyrimidine-8-thione **5a**,**b**, which were alkylated with ethyl iodide to give 8-ethylthio-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-7-phenyl-5,7-dihydrothiazolo[3,2-*a*]pyrimido[4,5-*d*]pyrimidine **6a**,**b**. Reaction of compound **6a**,**b** with hydrazine hydrate afforded 3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-7-phenyl-5,7-dihydro-8-hydrazinothiazolo-[3,2-*a*]pyrimido [4,5-*d*]pyrimidine **7a**,**b** (Scheme 1).

The *o*-amino carbohydrazide function of compound **4a**, **b** was exploited to synthesize further fused pyrimidine derivatives. Thus, reaction of **4a**,**b** with formic acid, acetic anhydride, and/or urea afforded 3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-7-*N*-formylamino-5,7-dihydro -5*H*-thiazolo[3,2-*a*]pyrimido[4,5-*d*]pyrimidine **8a**,**b**, 3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-8-methyl-7-*N*,*N*-diacetylamino-5,7-dihydrothiazolo [3,2-*a*]pyrimido[4,5-*d*]pyrimidine **9a**,**b,** and 3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-7-amino-7,9-dihydro-5*H*-thiazolo[3,2-*a*]pyrimido[4,5-*d*]pyrimidine-6,8-dione **10a**,**b** respectively.

Scheme 1



Reaction of carbohydrazide compound **4a**,**b** with acetylacetone or triethyl orthoformate gave 4-(7-amino-6-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimidin-3-yl)-3-methyl-1-phenyl-2-pyrazolin-5-one **11a**,**b** or 3-(3-methyl-5-oxo-1-phenyl-2-pyraz-olin-4-yl)-6-oxo-5-aryl-7-ethoxymethyleneamino-5,7-dihydro-5*H*-thiazolo[3,2-*a*]pyrimido[4,5-*d*]pyrimidine **12a**,**b** (Scheme 2).

Also, reaction of **4a**,**b** with nitrous acid gave 7-amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboazide **13a**,**b**, which refluxed with toluene underwent Curtius rearrangement to give 7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-9-aryl-2-oxo-1,3-dihydro-9*H*-imidazo[4,5-*d*]thiazolo[3,2-*a*]pyrimidine **14a**,**b**.

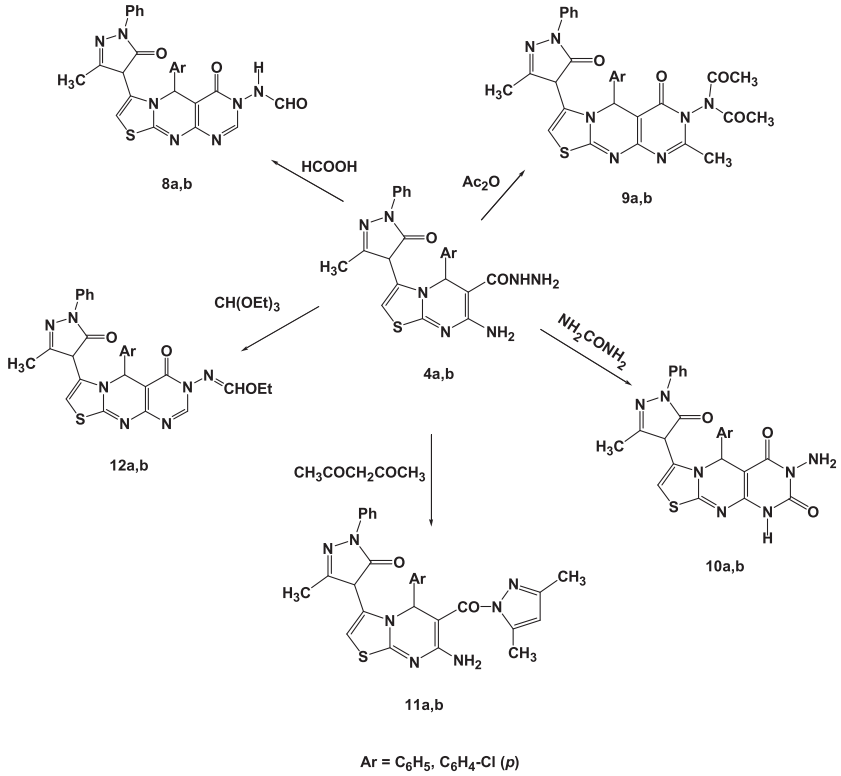
Condensation of **4a**,**b** with benzaldehyde in the presence of a catalytic amount of piperidine gave benzaldehyde,7-amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5*H*-thiazolo[3,2-*a*]- pyrimidine-6-carbohydrazone **15a**,**b**, which reacted with triethyl orthoformate to give 7-benzylideneamino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimido-[4,5-*d*] pyrimidine **16a**,**b** (Scheme 3).

The structure of new compounds was confirmed on the basis of elemental analyses and spectral data (^{1}H NMR, ^{13}C NMR, IR, and MS).

The biocidal activity of the synthesized compounds was tested against Gram-positive and Gram-negative bacteria as well as against yeast-like and filamentous fungi (Table 1). All microbes are potentially pathogenic especially for debilitated, malnourished, or immunosuppressed individuals. Different compounds showed varying antimicrobial action depending on the microorganism species and the compound itself. Compounds **2b**, **4b**, **5a**, and **8a** proved to be excellent candidates as antibacterial agents being able to inhibit all bacterial species tested. *Staphylococcus aureus* was the most sensitive organism being inhibited with ≤2.5 mg/mL of these compounds. Compounds **3a**, **6b**, **7a**, **9a**, and **10b** were also effective but often at higher concentrations ranging from 10–20 mg/mL. The rest of the tested compounds showed narrower spectrum of antibacterial activity.

Regarding the antifungal action, compounds **3a**, **4b**, **8a**, **8b**, and **9a** were inhibitory to most or all tested fungi with MICs ≤ 20 mg/mL. *Geotrichum candidum* (frequently reported to cause geotrichosis in human and animals) was sensitive to 12 out of the 20 compounds tested. *Aspergillus flavus* (a famous allergenic, pathogenic, and toxigenic mold) showed sensitivity to 7 compounds and was markedly inhibited by compound **8b** with MIC 10 mg/mL and high sensitive to **9a** with MIC 2.5 mg/mL. *Candida*

Scheme 2



albicans (cause of candidosis in humans and animals) and *Scopulariopsis brevicaulis* (often reported as a cause of nail infections) were also inhibited by some compounds as shown in Table 1. *Trichophyton rubrum* (usually involved in skin and nail infections) was successfully inhibited by compounds **3a**, **8b**, and **9a** at MIC of 20 mg/mL. *Fusarium oxysporum* (one of famous plant pathogens) was also sensitive to compounds **3a**, **4b**, **5a**, and **8b** (MICs between 10–20 mg/mL).

CONCLUSIONS

This investigation was directed toward the synthesis of novel pyrazolinyl thiazolopyrimidine and pyrazolinyl thiazolopyrimidopyrimidine derivatives by the reaction of amino ester derivatives with various reagents. The synthesized compounds were tested against some strains of bacteria and fungi and some of them exhibit antimicrobial activity.

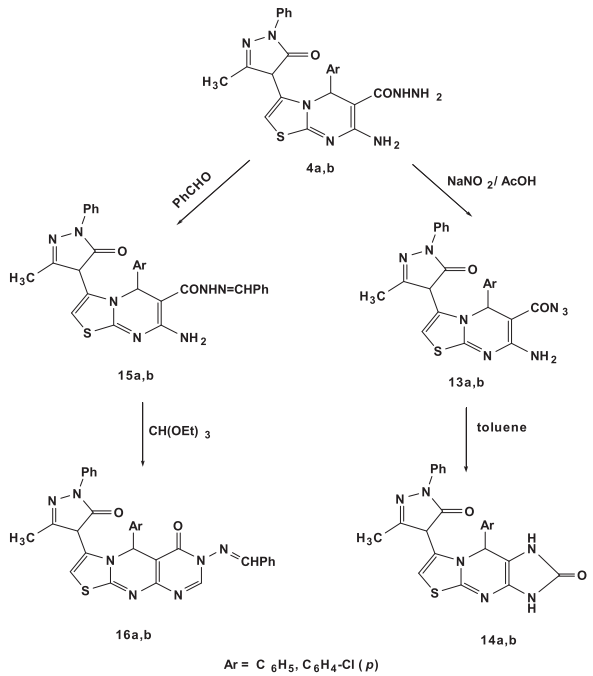
EXPERIMENTAL

Melting points were determined on APP. Digital ST 15 melting point apparatus and are uncorrected. Elemental analyses (C, H, N, S) were conducted using a Vario EL C, H, N, S Analyzer; their results were found to be in good agreement (±0.3%) with the calculated values. The IR spectra were obtained on a Pye-Unicam SP 3-100 spectrophotometer using the KBr disc technique (ν_{max} in cm^{1}). ^{1}H NMR spectra were recorded on EM 90 NMR spectrometer, and a varian ^{1}H-Gemini 400 spectrometer with chemical shifts expressed in δ ppm using TMS as the internal reference. ^{13}C NMR spectra were obtained on a varian ^{1}H-Gemini 400 spectrometer. The mass spectra were run on JOEL JMS 600 spectrometer.

7-Amino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenyl-5H-thiazolo[3,2-*a*] pyrimidine [16] (1a). A mixture of 4-(2-aminothiazol-4-yl)-3-methyl-5-oxo-1-phenyl-2-pyrazoline (10 mmol) and benzylidene ethyl cyanoacetate (10 mmol) in ethanol (30 mL) and piperidine (five drops) was refluxed for 10 h. The reaction mixture was poured into cold water, and the solid precipitate was collected, dried, and crystallized from toluene to give **1a**.

7-Amino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-*p*chlorophenyl-5H-thiazolo[3,2-*a*]pyrimidine (1b). A mixture of 4-(2-aminothiazol-4-yl)-3-methyl-5-oxo-1-phenyl-2-pyrazoline (10 mmol) and *p*-chlorobenzylidene ethyl cyanoacetate (10 mmol) in ethanol (30 mL) and piperidine (five drops) was refluxed for 10 h. The reaction mixture was poured into cold water and the solid precipitate was collected, dried, and crystallized from toluene to give pale yellow crystals, yield 3.65 g (72%), mp 286–288°C; IR (KBr): 3100–3250 (NH_2), 2915 (CH aliphatic), 1710 (CO ester), 1640 (CO pyrazolone) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.64–7.24 (m, 5H, phenyl protons), 7.15–7.00 (m, 4H, phenyl protons), 6.90 (s, thiazole-H), 6.70 (s, pyrimidine-H), 6.60 (s, pyrazolone-H), 5.40 (s, NH_2 exchangable with D_2O), 4.19 (q, J = 7.00 Hz, CH_2), 2.25 (s, pyrazolone CH_3), 1.20 (t, J = 7.00Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 170 (CO pyrazolone), 167 (CO ester), 162 (C═N pyrimidine), 159 and 105 (C═C

Scheme 3



pyrimidine), 157 (C═N pyrazolone), 154 (C thiazole), 141–127 (C and CH phenyl rings), 89 (CH thiazole), 60 (CH_2 ethyl), 50 (CH pyrazolone), 45 (CH pyrimidine), 18 (CH_3 pyrazolone), 14 (CH_3 ethyl) ppm. EI ms: m/z = 509.38 [M^++2] (15), 506.89 [M^+] (49), 473.01(35), 456.51 (24), 444.14 (41), 387.01(40), 316.12 (51), 271.92 (19), 174.00 (71), 37.05 (11), 35.27 (17).

7-Acetylamino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5H-thiazolo [3,2-*a*]pyrimidine 2a,b. A mixture of **1a** or **1b** (10 mmol) and acetyl chloride (5 mL) in pyridine (15 mL) was refluxed for 3 h. The reaction mixture was cooled, poured into cold water, and the solid separated product was filtered off to give **2a** and **2b**, respectively.

7-Acetylamino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenyl-5H-thiazolo [3,2-a]pyrimidine (2a). Crystallized from benzene to give white crystals, yield 3.86 g (72%), mp 210–212°C. IR (KBr): 3100–3250 (NH_2), 2915 (CH aliphatic), 1710 (CO ester), 1685 (CO acetyl), 1640 (CO pyrazolone) cm^{-1}. ^1H NMR ($CDCl_3$, 90 MHz): δ = 8.30 (s, NH exchangable with D_2O), 7.70–7.20 (m, 10H, phenyl protons), 7.00 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.80 (s, pyrazolone-H), 4.10 (q, J = 6.70 Hz, CH_2), 3.20 (s, CH_3 acetyl), 2.30 (s, pyrazolone-CH_3), 1.3 (t, J = 6.70 Hz, CH_3) ppm.

7-Acetylamino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-p-chlorophenyl-5H-thiazolo[3,2-a]pyrimidine (2b). Crystallized from benzene to give white powder, yield 3.74g (68%), mp 219–221°C. IR (KBr): 3100–3250 (NH_2), 2915 (CH aliphatic), 1710 (CO ester), 1685 (CO acetyl), 1640 (CO pyrazolone) cm^{-1}. ^1H NMR (DMSO-d_6, 90 MHz): δ = 8.20 (s, NH exchangable with D_2O), 7.70–7.40 (m, 9H, phenyl protons), 7.00 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.80 (s, pyrazolone-H), 4.10 (q, J = 10 Hz, CH_2), 3.20 (s, CH_3 acetyl), 2.30 (s, CH_3 pyrazolone), 1.3 (t, J = 10 Hz, CH_3) ppm.

7-Benzoylamino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5H-thiazolo [3,2-*a*]pyrimidine 3a,b. A mixture of **1a** or **1b** (10 mmol) and benzoyl chloride (5 mL) in pyridine (15 mL) was refluxed for 3 h. The reaction mixture was cooled and the solid product thus separated was filtered off, treated with pet. ether (60–80°C) and crystallized from the proper solvent to give **3a** and **3b**, respectively.

7-Benzoylamino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenyl-5H-thiazolo[3,2-a]pyrimidine (3a). Crystallized from ethanol to give pale brown powder, yield 4.04 g (70%), mp 215–217°C. IR (KBr): 3250 (NH exchangable with D_2O), 2915 (CH aliphatic), 1710 (CO ester), 1690 (CO benzoyl), 1640 (CO pyrazolone) cm^{-1}. ^1H NMR (DMSO-d_6, 90MHz): δ = 7.90 (s, NH exchangable with D_2O), 7.70–7.10 (m, 15H, phenyl protons), 7.00 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.80 (s, pyrazolone-H), 4.00 (q, J = 6.70 Hz, CH_2 ester), 2.30 (s, pyrazolone-CH_3), 1.20 (t, J = 6.70 Hz, CH_3 ester) ppm.

7-Benzoylamino-6-carboethoxy-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-p-chlorophenyl-5H-thiazolo[3,2-a]pyrimidine (3b). Crystallized from ethanol to give red powder, yield 4.28 g (70%), mp 200–202°C. IR (KBr): 3250 (NH), 2915 (CH aliphatic), 1710 (CO ester), 1690 (benzoyl), 1640 (pyrazolone) cm^{-1}. ^1H NMR (DMSO-d_6, 90MHz): δ = 7.90 (s, NH exchangable with D_2O), 7.70–7.20 (m, 14H, phenyl protons), 7.00 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.80 (s, pyrazolone-H), 4.00 (q, J = 6.60 Hz, CH_2 ester), 2.30 (s, CH_3-pyrazolone), 1.20 (t, J = 6.60 Hz, CH_3 ester) ppm.

7-Amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carbohydrazide 4a,b. A mixture of **1a** or **1b** (10 mmol) and hydrazine hydrate 98% (1.5 mL, 10 mmol) was refluxed for 2 h. The reaction mixture was cooled, and the solid thus formed was collected and crystallized from the proper solvent to give **4a** and **4b**, respectively.

7-Amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenyl-5H-thiazolo[3,2-a] pyrimidine-6-carbohydrazide (4a). Crystallized from ethanol to give white crystals, yield 3.08 g (67%), mp 270–272°C. ir (KBr): 3250–3450 ($NHNH_2$, NH_2), 1680 (CO carbohydrazide), 1635 (CO pyrazolone) cm^{-1}. ^1H NMR ($CDCl_3$,

Table 1

The minimum inhibitory concentrations of the compounds tested (mg/mL).

	2a	**2b**	**3a**	**3b**	**4a**	**4b**	**5a**	**5b**	**6a**	**6b**	**7a**	**7b**	**8a**	**8b**	**9a**	**9b**	**10a**	**10b**	**11a**	**11b**	Ref*
Bacteria																				–	
Bacillas cereus (*Gram* positive)	10	20	20	10	–	1.25	20	–	–	20	–	10	20	–	20	–	20	20	–	–	0.25
Staphylococcus aureus (*Gram* positive)	–	0.25	10	–	–	2.5	2.5	–	–	2.5	–	–	0.25	2.5	0.25	–	–	20	–	–	0.125
Pseudomonas aeruginosa (*Gram* negative)	–	20	–	–	–	2.5	20	–	20		20	–	20	–	20	–	–	20	–	–	5
Serratia marcescens (*Gram* negative)	20	2.5	20	–	–	10	20	–	–	10	20	10	10	20	–	–	–	20	20	20	1.25
Escherichia coli (*Gram* negative)	–	10	20	–	20	2.5	20	20	20	–	20	–	20	–	20	–	20	–	–	–	1.25
Fungi																					
Geotrichum candidum	–	–	20	–	–	10	–	–	–	20	–	–	–	20	10	20	20	20	20	20	2.5
Candida albicans	20	–	20	20	–	10	–	20	–	–	–	–	20	20	–	–	–	–	–	–	2.5
Fusarium oxysporum	–	–	20	–	–	10	20	–	–	–	–	–	–	–	20	–	–	–	–	–	2.5
Aspergillus flavus	–	–	–	–	–	20	20	–	–	20	–	–	20	10	2.5	–	–	20	–	–	2.5
Scopulariopsis brevicaulis	20	–	–	–	–	10	–	–	–	–	–	–	20	10	20	–	–	–	–	–	2.5
Trichophyton rubrum	–	–	20	–	–	–	–	–	–	–	–	–	–	20	20	–	–	–	–	–	2.5

*Ref. = Reference drugs = (chloramphenicol as antibacterial and clotrimazole as antifungal).
(–) = No antimicrobial action.

400 MHz): δ = 9.50 (s, NH exchangable with D_2O), 7.64–7.24 (m, 5H, phenyl protons), 7.19 (s, NH_2 exchangable with D_2O), 7.14–7.06 (m, 5H, phenyl protons), 6.90 (s, thiazole-H), 6.70 (s, pyrimidine-H), 6.60 (s, pyrazolone-H), 5.39 (s, NH_2 pyrimidine exchangable with D_2O), 2.21 (s, CH_3 pyrazolone) ppm. ^{13}C NMR ($CDCl_3$, 400 MHz): δ 170 (CO pyrazolone), 164 (CONH), 162 (C═N pyrimidine), 157 and 103 (C═C pyrimidine), 155 (C═N pyrazolone), 154 (C thiazole), 142–124 (C and CH phenyl rings), 89 (CH thiazole), 50 (CH pyrazolone), 45 (CH pyrimidine), 18 (CH_3 pyrazolone) ppm. EI ms: *m/z*: 458.79 [M^+] (67), 452.12 (24), 431.40 (23), 382.32 (42), 285.90 (59), 173 (71).

7-Amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-p-chlorophenyl-5H-thiazolo[3,2-a]-pyrimidine-6-carbohydrazide (4b). Crystallized from benzene to give pale yellow crystals, yield 3.19 g (65%), mp: 262–263°C. IR (KBr): 3250–3450 ($NHNH_2$, NH_2), 1680 (CO carbohydrazide), 1635 (CO pyrazolone) cm^{-1}. ^1H NMR (DMSO-d_6, 90 MHz): δ = 9.30 (s, NH exchangable with D_2O), 7.73–7.29 (m, 9H, phenyl protons), 7.19 (s, NH_2 exchangable with D_2O), 7.05 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.80 (s, pyrazolone-H), 5.39 (s, NH_2 pyrimidine exchangable with D_2O), 2.3 (s, CH_3 pyrazolone) ppm.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-7-phenyl-7,9-dihydro-5*H*-thiazolo-[3,2-*a*]pyrimido[4,5-*d*]pyrimidine-8-thione 5a,b. A mixture of **1 a**,**b** (10 mmol) and phenyl isothiocyanate (1.4 g, 10 mmol) in pyridine (30 mL) was refluxed for 8 h. The cooled reaction mixture was poured into ice water mixture, acidified with acetic acid, and the precipitated solid was collected and crystallized from the proper solvent to give **5a** and **5b**, respectively.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5,7-diphenyl-7,9-dihydro-5H-thiazolo- [3,2-a]pyrimido[4,5-d]pyrimidine-8-thione (5a). Crystallized from benzene to give pale green powder, yield 3.66 g (65%), mp 237–239°C. IR (KBr): 3250 (NH), 1695 (CO pyrimidine), 1635 (CO pyrazolone), 1510 (C═S) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 10.00 (s, NH exchangable with D_2O), 7.64–7.24 (m, 10H, phenyl protons), 7.14–7.06 (m, 5H, phenyl protons), 6.90 (s, thiazole-H), 6.80 (s, pyrimidine-H), 6.75 (s, pyrazolone-H), 2.20 (s, CH_3 pyrazolone) ppm. ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 178 (C═S pyrimidine), 170 (CO pyrazolone), 167 (C═O pyrimidine), 162 (C═N pyrimidine), 159 and 103 (C═C pyrimidine), 155 (C═N pyrazolone), 154 (C thiazole), 142–124 (C and CH phenyl rings), 89 (CH thiazole), 50 (CH pyrazolone), 45 (CH pyrimidine), 18 (CH_3 pyrazolone) ppm. EI ms: *m/z*: 562.21[M^+] (67), 527 (21), 485.41 (52), 173.12 (76), 77 (61).

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-p-chlorophenyl-7-phenyl-7,9-dihydro-5H-thiazolo[3,2-a]pyrimido [4,5-d]pyrimidine-8-thione (5b). Crystallized from benzene to give white crystals, yield 4.11g (69%) mp 245–247°C. IR (KBr): 2300 (NH), 1695 (CO pyrimidine), 1635 (CO pyrazolone), 1510 (C═S) cm^{-1}. ^1H NMR ($CDCl_3$, 90 MHz): δ = 10.00 (s, NH exchangable with D_2O), 7.74–7.30 (m, 14H, phenyl protons), 7.10 (s, thiazole-H), 7.00 (s, pyrimidine-H), 6.92 (s, pyrazolone-H), 2.20 (s, CH_3 pyrazolone) ppm.

8-Ethylthio-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-7-phenyl-5,7-dihydro thiazolo[3,2-*a*]pyrimido[4,5-*d*]pyrimidine 6a,b. To a solution of **5a** or **5b** (10 mmol) in hot ethanol containing sodium acetate (0.75 g, 10 mmol), ethyl iodide (1.56 mL, 10 mmol) was added with stirring for 3 h. The solid precipitate was collected, dried, and crystallized from the proper solvent to give **6a** and **6b**, respectively.

8-Ethylthio-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5,7-diphenyl-5,7-dihydro thiazolo [3,2-a]pyrimido[4,5-d] pyrimidine (6a). Crystallized from ethanol to give white crystals, yield 3.96 g (67%), mp 230–232°C. IR (KBr): disappearance of (NH), 2950 (CH aliphatic), 1695 (CO pyrimidine), 1640 (CO pyrazolone) cm^{-1}. ^1H NMR ($CDCl_3$, 90 MHz): δ = 8.10–7.50 (m, 15H, phenyl protons), 7.00 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.80 (s, pyrazolone-H), 4.10 (q, *J* = 6.7Hz, CH_2), 2.20 (s, CH_3 pyrazolone), 1.00 (t, *J* = 6.7Hz, CH_3) ppm; EI ms: *m/z*: 590.32 [M^+] (49), 559.12 (68), 173.12 (76), 77 (61), 29 (12).

Table 2

The elemental analyses of the prepared compounds.

Compound	Formula		Elemental analyses				
			C	H	N	S	Cl
1b	$C_{25}H_{22}N_5O_3SCl$	Calcd.	59.11	4.37	13.79	6.31	6.98
		Found	58.89	4.24	13.67	6.21	6.81
2a	$C_{27}H_{24}N_5O_4SCI$	Calcd.	62.90	4.89	13.58	6.22	–
		Found	62.74	4.75	13.34	6.16	–
2b	$C_{27}H_{25}N_5O_4SCl$	Calcd.	58.96	4.40	12.73	5.83	6.45
		Found	58.82	4.28	12.61	5.71	6.30
3a	$C_{32}H_{27}N_5O_4S$	Calcd.	66.54	4.71	12.12	5.55	–
		Found	66.34	4.61	12.06	5.48	–
3b	$C_{32}H_{26}N_5O_4SCl$	Calcd.	62.79	4.28	11.44	5.24	5.79
		Found	62.68	4.16	11.32	5.10	5.66
4a	$C_{23}H_{21}N_7O_2S$	Calcd.	60.12	4.61	21.34	6.98	–
		Found	60.01	4.46	21.21	6.87	–
4b	$C_{23}H_{20}N_7O_2SCl$	Calcd.	55.92	4.08	19.85	6.49	7.18
		Found	55.81	3.98	19.71	6.36	7.05
5a	$C_{30}H_{22}N_6O_2S_2$	Calcd.	64.04	3.94	14.94	11.40	–
		Found	63.91	3.72	14.81	11.65	–
5b	$C_{30}H_{21}N_6O_2S_2Cl$	Calcd.	60.34	3.54	14.07	10.74	5.94
		Found	60.25	3.43	13.94	10.61	5.84
6a	$C_{32}H_{26}N_6O_2S_2$	Calcd.	65.06	4.44	14.23	10.86	–
		Found	64.97	4.37	14.20	10.80	–
6b	$C_{32}H_{25}N_6O_2S_2Cl$	Calcd.	61.48	4.03	13.44	10.26	5.67
		Found	61.40	3.91	13.32	10.14	5.56
7a	$C_{30}H_{24}N_8O_2S$	Calcd.	64.27	4.31	19.99	5.72	–
		Found	64.16	4.25	19.90	5.63	–
7b	$C_{30}H_{23}N_8O_2SCl$	Calcd.	60.55	3.90	18.83	5.39	5.96
		Found	60.48	3.76	18.71	5.31	5.85
8a	$C_{25}H_{19}N_7O_3S$	Calcd.	60.35	3.85	19.71	6.45	–
		Found	60.29	3.78	19.64	6.36	–
8b	$C_{25}H_{18}N_7O_3SCl$	Calcd.	56.44	3.41	18.43	6.03	6.66
		Found	56.36	3.35	18.32	5.93	6.57
9a	$C_{29}H_{25}N_7O_4S$	Calcd.	61.36	4.44	17.27	5.65	–
		Found	61.30	4.36	17.18	5.52	–
9b	$C_{29}H_{24}N_7O_4Cl$	Calcd.	57.85	4.02	16.29	5.33	5.89
		Found	57.80	3.92	16.20	5.25	5.82
10a	$C_{24}H_{19}N_7O_3S$	Calcd.	59.37	3.94	20.19	6.60	–
		Found	59.24	3.97	20.12	6.51	–
10b	$C_{24}H_{18}N_7O_3S$ Cl	Calcd	55.44	3.49	18.86	6.17	6.82
		Found	55.32	3.41	18.75	6.08	6.71
11a	$C_{28}H_{25}N_7O_2S$	Calcd.	64.23	4.81	18.73	6.12	–
		Found	64.28	4.64	18.61	6.17	–
11b	$C_{28}H_{24}N_7O_2SCl$	Calcd.	60.26	4.33	17.57	5.73	6.35
		Found	60.18	4.40	17.45	5.66	6.26
12a	$C_{27}H_{23}N_7O_3S$	Calcd.	61.70	4.41	18.65	6.10	–
		Found	61.58	4.34	18.54	6.01	–
12b	$C_{27}H_{22}N_7O_3SCl$	Calcd.	57.91	3.96	17.51	5.73	6.33
		Found	57.86	3.87	17.43	5.65	6.21
13a	$C_{23}H_{18}N_8O_2S$	Calcd.	58.71	3.86	23.82	6.82	–
		Found	58.62	3.74	23.71	6.70	–
13b	$C_{23}H_{17}N_8O_2SCl$	Calcd.	54.71	3.39	22.19	6.35	7.02
		Found	54.60	3.31	22.10	6.40	6.90
14a	$C_{23}H_{18}N_6O_2S$	Calcd.	62.43	4.10	18.99	7.25	–
		Found	62.34	4.01	18.87	7.14	–
14b	$C_{23}H_{17}N_6O_2SCl$	Calcd.	57.92	3.59	17.62	6.72	7.43
		Found	57.83	3.49	17.53	6.64	7.34
15a	$C_{30}H_{25}N_7O_2S$	Calcd.	65.80	4.60	17.90	5.86	–
		Found	65.71	4.52	17.79	5.71	–
15b	$C_{30}H_{24}N_7O_2SCl$	Calcd.	61.90	4.16	16.84	5.51	6.09
		Found	62.18	4.03	16.73	5.39	5.88
16a	$C_{31}H_{23}N_7O_2S$	Calcd.	66.77	4.16	17.58	5.75	–
		Found	66.66	4.11	17.47	5.63	–
16b	$C_{31}H_{22}N_7O_2SCl$	Calcd.	62.89	3.75	16.56	5.42	5.99
		Found	62.78	3.69	16.50	5.34	5.84

8-Ethylthio-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-p-chlorophenyl-7-phenyl-5,7-dihydrothiazolo[3,2-a]pyrimido [4,5-d]pyrimidine (6b). Crystallized from ethanol to give yellow crystals, yield 4.06 g (65%), mp 240–242°C. IR (KBr): 2915 (CH aliphatic), 1695 (CO pyrimidine), 1640 (CO pyrazolone) cm^{-1}. ^1H NMR (DMSO-d_6, 90MHz): δ = 8.00–7.30 (m, 14H, phenyl protons), 7.00 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.80 (s, pyrazolone-H), 4.10 (q, J = 10 Hz, CH_2), 2.20 (s, CH_3 pyrazolone), 1.00 (t, J = 10 Hz, CH_3) ppm.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-7-phenyl-5,7-dihydro-8-hydrazino thiazolo[3,2-*a*]pyrimido[4,5-*d*] pyrimidine 7a,b. To a solution of **6a** or **6b** (10 mmol) in pyridine (30 mL), hydrazine hydrate 98% (0.49 mL, 10 mmol) was added and the reaction mixture was refluxed for 2 h. The product thus formed was filtered-off, dried, and crystallized from the proper solvent to give **7a** and **7b**, respectively.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5,7-diphenyl-5,7-dihydro-8-hydrazinohiazolo[3,2-a]pyrimido[4,5-d] pyrimidine (7a). Crystallized from benzene to give pale yellow crystals, yield 3.92 g (55%), mp 245–247°C. IR (KBr): 3400–3150 ($NHNH_2$), 1690 (CO pyrimidine), 1630 (CO pyrazolone) cm^{-1}; ^1H NMR (DMSO-d_6, 90 MHz): δ = 10.40 (s, NH exchangable with D_2O), 7.90–7.30 (m, 15H, phenyl protons), 7.10 (s, thiazole-H), 7.00 (s, pyrimidine-H), 6.90 (s, pyrazolone-H), 5.50 (s, NH_2 exchangable with D_2O), 2.20 (s,CH_3 pyrazolone) ppm. EI ms: *m/z*: 559.72 [M^+] (71), 544.13 (21), 483.12 (53), 329.10 (15), 173.12 (76), 77 (61).

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-p-chlorophenyl-7-phenyl-5,7-dihydro-8-hydrazinothiazolo[3,2-a] pyrimido[4,5-d]pyrimidine (7b). Crystallized from ethanol to give yellow crystals, yield 4.16 g (70%), mp 251–253°C. IR (KBr): 3400–3150 ($NHNH_2$), 1690 (CO pyrimidine), 1630 (CO pyrazolone) cm^{-1}. ^1H NMR (DMSO-d_6, 90 MHz): δ = 10.40 (s, NH exchangable with D_2O), 7.90–7.20 (m, 14H, phenyl protons), 7.00 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.81 (s, pyrazolone-H), 5.50 (s, NH_2 exchangable with D_2O), 2.20 (s, CH_3 pyrazolone) ppm.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-7-*N*-formylamino-5,7-dihydro-5*H*-thiazolo[3,2-*a*]pyrimido[4,5-*d*]pyrimidine 8a,b. A mixture of **4a** or **4b** (10 mmol) with formic acid (20 mL) was refluxed for 4 h. The precipitate thus formed after cooling was collected, dried, and crystallized from the proper solvent to give **8a** and **8b**, respectively.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-phenyl-7-N-formylamino-5,7-dihydro-5H-thiazolo[3,2-a]pyrimido[4,5-d] pyrimidine (8a). Crystallized from ethanol to give white powder, yield 3.39 g (68%), mp 215–217°C. IR (KBr): 3350 (NH), 1705 (CO formyl), 1690 (CO pyrimidine), 1645 (CO pyrazolone) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 10.80 (s, NH exchangable with D_2O), 8.51 (s, formyl-H), 7.72 (s, pyrimidine-H), 7.64–7.24 (m, 5H, phenyl protons), 7.14–7.06 (m, 5H, phenyl protons), 7.00 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.76 (s, pyrazolone-H), 2.23 (s, CH_3 pyrazolone) ppm. ^{13}C NMR (DMSO-d_6, 400 MHz): δ = 170 (CO pyrazolone), 167 (C═O pyrimidine), 165 (CHO), 163 (CH═N pyrimidine), 161 (C═N pyrimidine), 159 and 103 (C═C pyrimidine), 155 (C═N pyrazolone), 154 (C thiazole), 142–124 (C and CH phenyl rings), 89 (CH thiazole), 50 (CH pyrazolone), 45 (CH pyrimidine), 18 (CH_3 pyrazolone) ppm. EI ms: *m/z*: 497.02 [M^+] (72), 479.01 (49), 469.11(39), 173.12 (76), 77 (61), 28 (5), 18 (10).

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-p-chlorophenyl-7-N-formylamino-5,7-dihydro-5H-thiazolo[3,2-a] pyrimido[4,5-d]pyrimidine (8b). Crystallized from ethanol to give pale yellow crystals, yield 3.49 g (68%), mp 222–224°C. IR (KBr): 3350 (NH), 1705 (CO formyl), 1690 (CO pyrimidine), 1645 (CO pyrazolone) cm^{-1}. ^1H NMR ($CDCl_3$, 90 MHz): δ = 10.80 (s, NH exchangable with D_2O), 8.60 (s, formyl-H), 8.00 (s, pyrimidine-H), 7.60–7.20 (m, 9H, phenyl protons), 7.00 (s, thiazole-H), 6.80 (s, pyrimidine-H), 6.60 (s, pyrazolone-H), 2.30 (s, CH_3 pyrazolone) ppm.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-8-methyl-7-*N*,*N*-diacetylamino-5,7-dihydrothiazolo[3,2-*a*] pyrimido[4,5-*d*]pyrimidine 9a,b. A mixture of **4a** or **4b** (10 mmol) and acetic anhydride (20 mL) was refluxed for 3 h. The reaction mixture was diluted with water and allowed to stand at room temperature for 1 h. The precipitate thus obtained was collected, dried, and crystallized from the proper solvent to give **9a** and **9b**, respectively.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-phenyl-8-methyl-7-N,N-diacetylamino-5,7-dihydrothiazolo[3,2-a]pyrimido [4,5-d]pyrimidine (9a). Crystallized from ethanol to give white crystals, yield 3.92 g (69%), mp 240–242°C. IR (KBr): 3000–2915 (CH aliphatic), 1760–1690 (2CO acetyl), 1645 (CO pyrazolone) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.64–7.24 (m, 5H, phenyl protons), 7.14–7.06 (m, 5H, phenyl protons), 6.92 (s, thiazole-H), 6.80 (s, pyrimidine-H), 6.71 (s, pyrazolone-H), 2.40 (s, $2CH_3$), 2.20 (s, CH_3 pyrazolone), 1.20 (s, CH_3 pyrimidine) ppm. ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 175 (2CO acetyl), 170 (CO pyrazolone), 167 (C═O pyrimidine), 164 (CH═N pyrimidine), 161 (C═N pyrimidine), 159 and 103 (C═C pyrimidine), 155 (C═N pyrazolone), 154 (C thiazole), 142–124 (C and CH phenyl rings), 89 (CH thiazole), 50 (CH pyrazolone), 45 (CH pyrimidine), 18 (CH_3 pyrazolone), 14 (CH_3 pyrimidine), 16 ($2CH_3$ acetyl) ppm. EI ms: *m/z*: 566.96 [M^+] (69), 524.38 (10), 481.30 (15), 173.12 (76), 77 (61).

3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-p-chlorophenyl-8-methyl-7-N,N-diacetylamino-5,7-dihydrothiazolo[3,2-a]pyrimido [4,5-d] pyrimidine (9b). Crystallized from ethanol to give yellow powder, yield 4.15 g (69%), mp 253–255°C. IR (KBr): 3000–2915 (CH aliphatic), 1760–1690 (2CO acetyl), 1645 (CO pyrazolone) cm^{-1}. ^1H NMR (DMSO-d_6, 90 MHz): δ = 7.60–7.20 (m, 9H, phenyl protons), 7.00 (s, thiazole-H), 6.82 (s, pyrimidine-H), 6.60 (s, pyrazolone-H), 2.40 (s, $2CH_3$), 2.26 (s, CH_3 pyrazolone), 1.20 (s, CH_3 pyrimidine) ppm.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-7-amino-7,9–dihydro-5*H*-thiazolo[3,2-*a*]-pyrimido[4,5-*d*]pyrimidine-6,8-dione 10a,b. A mixture of **4a** or **4b** (10 mmoles) and urea (0.6 g, 10 mmol) was refluxed in decalin (30 mL) for 3 h. The solid product thus obtained on cooling was filtered off, washed with pet. ether 60–80 and crystallized from the proper solvent to give **10a** and **10b**, respectively.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenyl-7-amino-7,9–dihydro-5H-thiazolo [3,2-a]pyrimido[4,5-d]pyrimidine-6,8-dione (10a). Crystallized from benzene to give white crystals, yield 2.80 g (68%), mp 271–273°C; IR (KBr): 3400 (NH_2), 3150 (NH), 1720–1695 (2 C═O pyrimidine), 1640 (C═O pyrazolone) cm^{-1}. ^1H NMR (DMSO-d_6, 400MHz): δ = 10.50 (s, NH exchangable with D_2O), 9.70 (s, NH_2 exchangable with D_2O), 7.64–7.24 (m, 5H, phenyl protons), 7.14–7.06 (m, 5H, phenyl protons), 6.95 (s, thiazole-H), 6.85 (s, pyrimidine-H), 6.71 (s, pyrazolone-H), 2.25 (s, CH_3

pyrazolone) ppm; ^{13}C NMR (DMSO-d_6, 400 MHz): δ = 170 (CO pyrazolone), 167 (C═O pyrimidine), 161 (C═N pyrimidine), 159 and 103 (C═C pyrimidine), 155 (C═N pyrazolone), 154 (C thiazole), 150 (C═O pyrimidine), 142–124 (C and CH phenyl rings), 89 (CH thiazole), 50 (CH pyrazolone), 45 (CH pyrimidine), 18 (CH_3 pyrazolone) ppm. EI ms: *m/z*: 484.80 [M^+] (80), 469.45 (71), 467.13 (34), 331.10 (24), 173.12 (76), 77 (61).

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-p-chlorophenyl-7-amino-7,9-dihydro-5H-thiazolo[3,2-a]pyrimido[4,5-d]pyrimidine-6,8-dione (10b). Crystallized from ethanol to give brown powder, yield 3.38 g (65%), mp 265–267°C. IR (KBr): 3400 (NH_2), 3150 (NH), 1720–1695 (2 C═O pyrimidine), 1640 (C═O pyrazolone) cm^{-1}. ^{1}H NMR (DMSO-d_6, 90 MHz): δ = 10.70 (s, NH exchangable with D_2O), 9.70 (s, NH_2 exchangable with D_2O), 7.60–7.20 (m, 9H, phenyl protons), 7.00 (s, thiazole-H), 6.90 (s, pyrimidine-H), 6.70 (s, pyrazolone-H), 2.20 (s, CH_3 pyrazolone) ppm.

4-(7-Amino-6-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimidin-3-yl)-3-methyl-1-phenyl-2-pyrazolin-5-one 11a,b. A mixture of **4a** or **4b** (10 mmol) and acetyl acetone (1.00 g, 10 mmol) in ethanol (30 mL) was refluxed for 3 h. On cooling, the formed solid product was filtered-off, dried, and crystallized from the proper solvent to give **11a** and **11b**, respectively.

4-(7-Amino-6-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-5-phenyl-5H-thiazolo[3,2-a]pyrimidin- 3-yl)-3-methyl-1-phenyl-2-pyrazolin-5-one (11a). Crystallized from benzene to give yellow powder, yield 3.46 g (66%), mp 230–232°C. IR (KBr): 3300–3100 (NH_2), 2960 (CH aliphatic), 1660 (CO pyrimidine), 1640 (CO pyrazolone) cm^{-1}. ^{1}H NMR (DMSO-d_6, 90 MHz): δ = 7.95–7.30 (m, 10H, phenyl protons), 7.20 (s, thiazole-H), 7.10 (s, pyrimidine-H), 7.00 (s, pyrazolone-H), 6.85 (s, pyrazole-H), 5.40 (s, NH_2 exchangable with D_2O), 2.20 (s, CH_3), 2.10 (s, $2CH_3$ pyrazole) ppm.

4-(7-Amino-6-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-5-p-chlorophenyl-5H-thiazolo[3,2-a]- pyrimidin-3-yl)-3-methyl-1-phenyl-2-pyrazolin-5-one (11b). Crystallized from benzene to give pale yellow crystals, yield 3.91 g (70%), mp 249–250°C. IR (KBr): 3300–3100 (NH_2), 2960 (CH aliphatic), 1660 (CO pyrimidine), 1640 (CO pyrazolone) cm^{-1}; ^{1}H NMR (DMSO-d_6, 90 MHz): δ = 8.00–7.40 (m, 9H, phenyl protons), 7.20 (s, thiazole-H), 7.11 (s, pyrimidine-H), 7.10 (s, pyrazolone-H), 6.90 (s, pyrazole-H), 5.40 (s, NH_2 exchangable with D_2O), 2.20 (s, CH_3), 2.10 (s, $2CH_3$ pyrazole) ppm.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-7-ethoxymethyleneamino-5,7-dihydro-thiazolo[3,2-*a*]pyrimido [4,5-*d*]pyrimidine 12a,b. A mixture of **4a** or **4b** (5 mmoles) and triethyl orthoformate (20 mL) was refluxed for 3 h. The solid precipitate thus formed on cooling was collected, dried, and crystallized from the proper solvent to give **12a** and **12b**, respectively.

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-phenyl-7-ethoxymethyleneamino-5,7-dihydro-thiazolo[3,2-a]pyrimido [4,5-d]pyrimidine (12a). Crystallized from ethanol to give white needles, yield 1.81 g (69%), mp 238–239°C. IR (KBr): 2960 (CH aliphatic), 1680 (CO pyrimidine), 1635 (CO pyrazolone), 1580 (C═N) cm^{-1}. ^{1}H NMR (DMSO-d_6, 90MHz): δ = 7.90–7.50 (m, 10H, phenyl protons and N═CH), 7.50 (s, pyrimidine-H), 7.20 (s. thiazole-H), 7.00 (s, pyrimidine-H), 6.90 (s, pyrazolone-H), 4.00 (q, *J* = 6.7 Hz, CH_2), 2.40 (s, CH_3 pyrazolone), 1.3 (t, *J* = 6.7Hz, CH_3) ppm. EI ms: *m/z*: 525.05 [M^+] (69), 479.16 (42), 173.12 (76), 77 (61), 46 (12) 44.12 (5).

3-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-p-chlorophenyl-7-ethoxymethyleneamino-5,7-dihydro-thiazolo [3,2-a]pyrimido[4,5-d] pyrimidine (12b). Crystallized from ethanol to give white crystals, yield 1.96 g (70%), mp 240–241° C. IR (KBr): 2960 (CH aliphatic), 1680 (CO pyrimidine), 1635 (CO pyrazolone), 1580 (C═N) cm^{-1}. ^{1}H NMR (DMSO-d_6, 90 MHz): δ = 7.90–7.60 (m, 9H, phenyl protons and N═CH), 7.50 (s, pyrimidine-H), 7.20 (s, thiazole-H), 7.00 (s, pyrimidine-H), 6.90 (s, pyrazolone-H), 4.00 (q, *J* = 6.7 Hz, CH_2), 2.40 (s, CH_3 pyrazolone), 1.3 (t, *J* = 6.7 Hz, CH_3) ppm. EI ms: *m/z*: 561.62 [M^++2] (23), 559.53 [M^+] (76), 173.12 (76), 77 (61), 37.20 (9), 35.10 (19).

7-Amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboazide 13a,b. To a cold solution of **4a** or **4b** (10 mmol) in glacial acetic acid (30 mL), sodium nitrite solution (0.69 g, 10 mmol) in water (5 mL) was added dropwise with stirring during 10 min at room temperature. The formed precipitate was collected, dried, and crystalized from the proper solvent to give **13a** and **13b**, respectively.

7-Amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenyl-5H-thiazolo[3,2-a]- pyrimidine-6-carboazide (13a). Crystallized from benzene to give brown crystals, yield 3.38 g (72%), mp 210–212°C. IR (KBr): 3400–3200 (NH_2), 2960 (CH aliphatic), at 2270 appearance of azide group (N_3), 1695 (CO), 1620 (CO pyrazolone) cm^{-1}. ^{1}H NMR (DMSO-d_6, 90MHz): δ = 8.00–7.30 (m, 10H, phenyl protons), 7.10 (s, thiazole-H), 7.00 (s, pyrimidine-H), 6.90 (s, pyrazolone-H), 5.50 (s, NH_2 exchangable with D_2O), 2.30 (s, CH_3) ppm.

7-Amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-p-chlorophenyl-5H-thiazolo[3,2-a]- pyrimidine-6-carboazide (13b). Crystallized from benzene to give red crystals, yield 3.58 g (71%), mp 215–217°C; IR (KBr): 3400, 3200 (NH_2), 2960 (CH aliphatic), at 2270 appearance of azide group (N_3), 1695 (CO), 1625 (CO pyrazolone) cm^{-1}. ^{1}H NMR (DMSO-d_6, 90 MHz): δ = 8.10–7.20 (m, 9H, phenyl protons), 7.10 (s, thiazole-H), 7.00 (s, pyrimidine-H), 6.90 (s, pyrazolone-H), 5.50 (s, NH_2 exchangable with D_2O), 2.30 (s, CH_3 pyrazolone) ppm.

7-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-9-aryl-2-oxo-1,3-dihydro-9*H*-imidazo[4,5-*d*]-thiazolo[3,2-*a*]pyrimidine 14a,b. The carboazide **13** (5 mmol) was heated under reflux for 3 h in dry toluene (30 mL). The reaction mixture was cooled whereby a precipitated solid was formed. It was collected and crystallized from the proper solvent to give **14a** and **14b**, respectively.

7-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-9-phenyl-2-oxo-1,3-dihydro-9H-imidazo[4,5-d]-thiazolo[3,2-a]pyrimidine (14a). Crystallized from dioxane to give yellow crystals, yield 1.61 g (73%), mp 245–246°C. IR (KBr): 3400–3310 (2NH), disappearance of azide and amino groups, 1680 (CO), 1630 (CO pyrazolone) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 11.10 (s, 2NH exchangable with D_2O), 7.64–7.24 (m, 5H, phenyl protons), 7.14–7.06 (m, 5H, phenyl protons), 6.95 (s, thiazole-H), 6.85 (s, pyrimidine-H), 6.71 (s, pyrazolone-H), 2.25 (s, CH_3 pyrazolone) ppm. ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 170 (CO pyrazolone), 161 (C═N pyrimidine), 155 (C═N pyrazolone), 154 (C thiazole), 142–124 (C and CH phenyl rings), 111 and 107 (C═C pyrimidine), 89 (CH thiazole), 50 (CH pyrazolone), 45 (CH pyrimidine), 18 (CH_3 pyrazolone) ppm.

7-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-9-p-chlorophenyl-2-oxo-1,3-dihydro-9H-imidazo[4,5-d]thiazolo[3,2-a]pyrimidine (14b). Crystallized from dioxane to give pale yellow crystals, yield 1.72 g (72%), mp 248–250°C. IR (KBr): 3400–3300 (2NH), disappearance of azide and amino groups, 1680 (CO), 1630 (CO pyrazolone) cm^{-1}. ^1H NMR (DMSO-d_6, 90 MHz): δ = 11.10 (s, 2NH exchangable with D_2O), 7.60–7.20 (m, 9H, phenyl protons), 7.00 (s, thiazole-H), 6.82 (s, pyrimidine-H), 6.60 (s, pyrazolone-H), 2.30 (s, CH_3 pyrazolone) ppm.

Benzaldehyde,7-amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-aryl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carbohydrazone 15a,b. A mixture of **4a** or **4b** (10 mmol) and benzaldehyde (10 mmol) in ethanol (30 mL) containing few drops of piperidine was refluxed for 3 h. The solid thus formed was collected and crystallized from the proper solvent to give **15a** and **15b**, respectively.

Benzaldehyde,7-amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenyl-5H-thiazolo-[3,2-a]pyrimidine-6-carbohydrazone (15a). Crystallized from dioxane to give yellow powder, yield 3.83 g (70%), mp 250–251°C; IR (KBr): 3350–3250 (NH, NH_2), 1660 (CO pyrimidine), 1640 (CO pyrazolone), 1580 (C═N) cm^{-1}. ^1H NMR (DMSO-d_6, 90 MHz): δ =11.10 (s, NH exchangable with D_2O), 9.50 (s, CH), 8.00–7.40 (m, 15H, phenyl protons) 7.10 (s, thiazole-H), 6.90 (s, H-pyrimidine), 6.80 (s, pyrazolone-H), 5.40 (s, NH_2 exchangable with D_2O), 2.30 (s, CH_3 pyrazolone) ppm.

Benzaldehyde,7-amino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-p-chlorophenyl-5H-thiazolo[3,2-a]pyrimidine-6-carbohydrazone (15b). Crystallized from dioxane to give pale yellow crystals, yield 4.25 (73%), mp 255–257°C; IR (KBr): 3350–3250 (NH, NH_2), 1660 (CO pyrimidine), 1640 (CO pyrazolone), 1580 (C═N) cm^{-1}. ^1H NMR (DMSO-d_6, 90 MHz): δ = 11.10 (s, NH exchangable with D_2O), 9.50 (s, CH), 8.10–7.40 (m, 14H, phenyl protons), 7.10 (s, thiazole-H), 7.00 (s, pyrimidine-H), 6.85 (s, pyrazolone-H), 5.40 (s, NH_2 exchangable with D_2O), 2.30 (s, CH_3 pyrazolone) ppm.

7-Benzylideneamino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-aryl-5*H*-thiazolo- [3,2-*a*]pyrimido[4,5-*d*]pyrimidine 16a,b. A mixture of **15a** or **15b** (5 mmol), triethyl orthoformate (5 mmol), and acetic anhydride (15 mL) was refluxed for 3 h. The solid precipitate thus formed on cooling was collected, dried, and crystallized from the proper solvent to give **16a** and **16b**, respectively.

7-Benzylideneamino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-phenyl-5H-thiazolo [3,2-a]pyrimido[4,5-d]pyrimidine (16a). Crystallized from dioxane to give pale brown powder, yield 1.92 g (69%), mp 262–264°C. IR (KBr): 1680 (CO pyrimidine), 1630 (CO pyrazolone), 1580 (C═N) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.20 (s, CH), 7.76 (s, pyrimidine-H), 7.64–7.06 (m, 15H, phenyl protons), 6.95 (s, thiazole-H), 6.85 (s, pyrimidine-H), 6.71 (s, pyrazolone-H), 2.25 (s, CH_3 pyrazolone) ppm. ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 170 (CO pyrazolone), 167 (C═O pyrimidine), 163 (CH═N pyrimidine), 161 (C═N pyrimidine), 159 and 103 (C═C pyrimidine), 157 (N═CH), 155 (C═N pyrazolone), 154 (C thiazole), 142–124 (C and CH phenyl rings), 89 (CH thiazole), 50 (CH pyrazolone), 45 (CH pyrimidine), 18 (CH_3 pyrazolone) ppm.

7-Benzylideneamino-3-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-6-oxo-5-p-chlorophenyl-5H-thiazolo[3,2-a]pyrimido[4,5-d] pyrimidine (16b). Crystallized from dioxane to give yellow powder, yield 2.07 g (70%), mp 259–261°C. IR (KBr): 1680 (CO pyrimidine), 1630 (CO pyrazolone), 1580 (C═N) cm^{-1}. ^1H NMR ($CDCl_3$, 90 MHz): δ = 8.30 (s, CH), 7.78 (s, pyrimidine-H), 7.67–7.10 (m, 14H, phenyl protons), 7.00 (s, thiazole-H), 6.82 (s, pyrimidine-H), 6.60 (s, pyrazolone-H), 2.30 (s, CH_3 pyrazolone) ppm.

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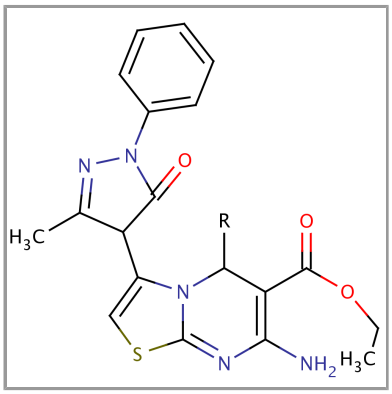
1



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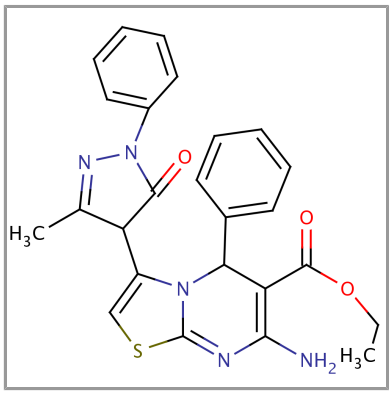

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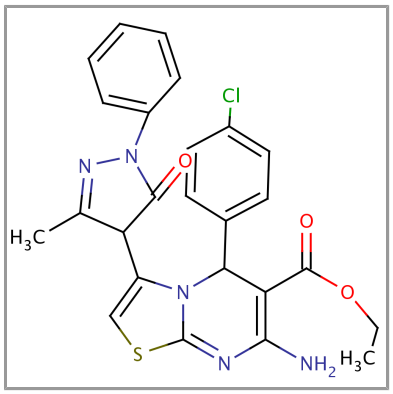

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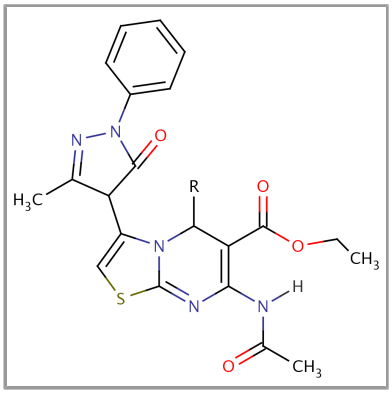

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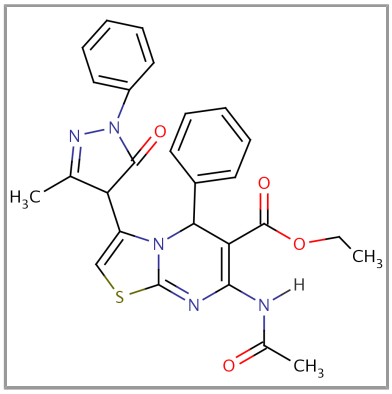

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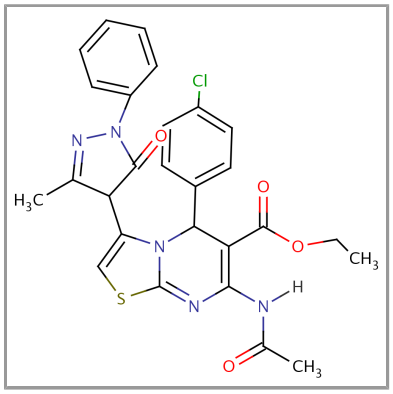

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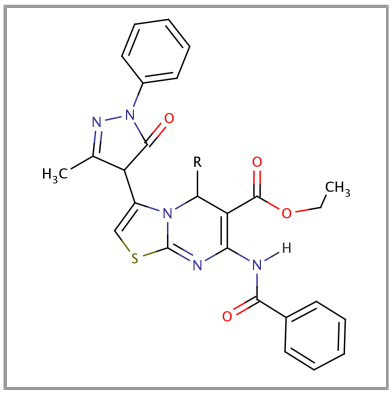

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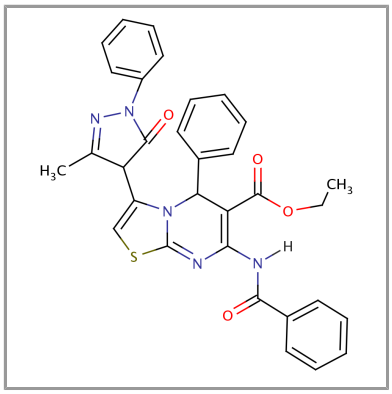

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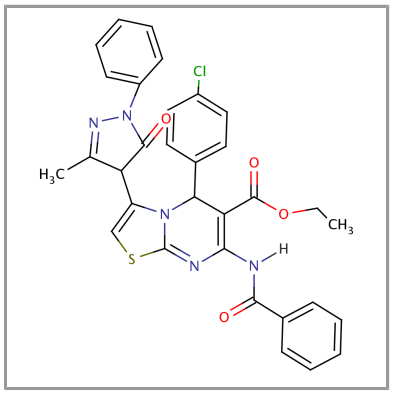

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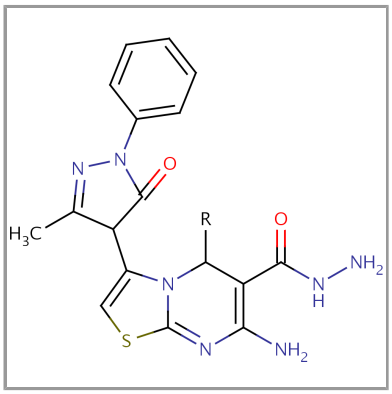

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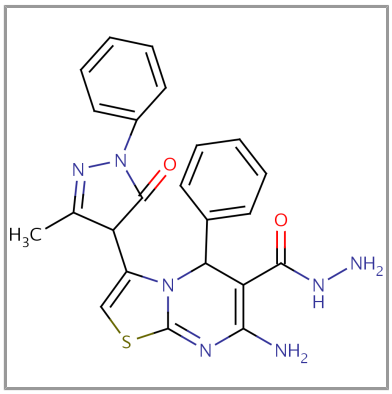

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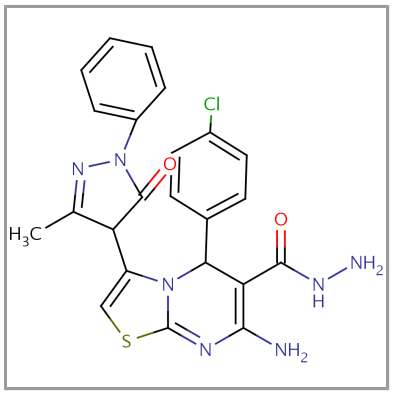

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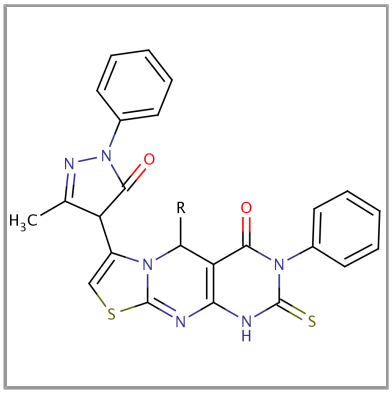

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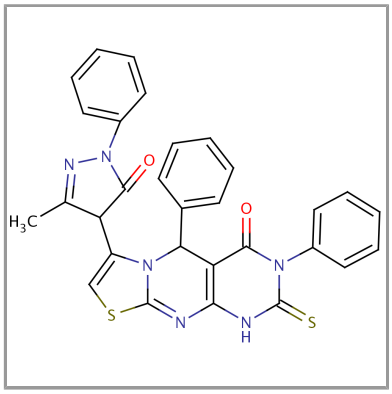

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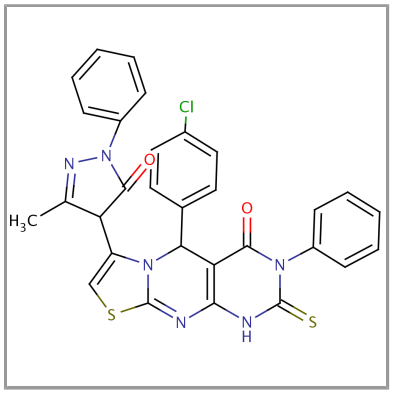

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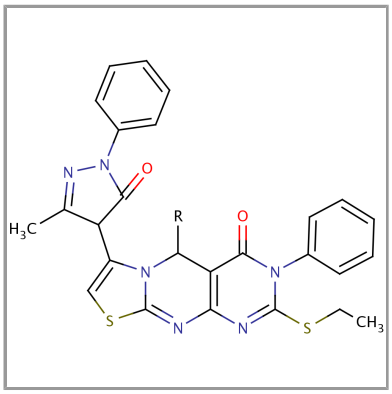

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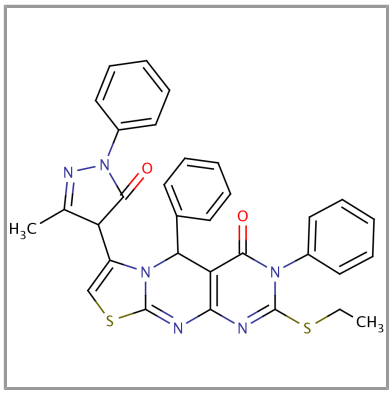

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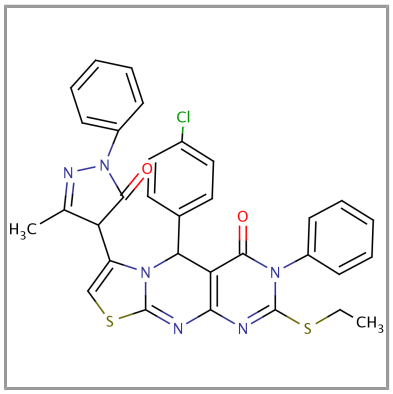

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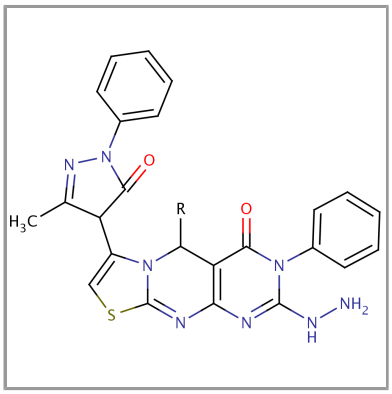

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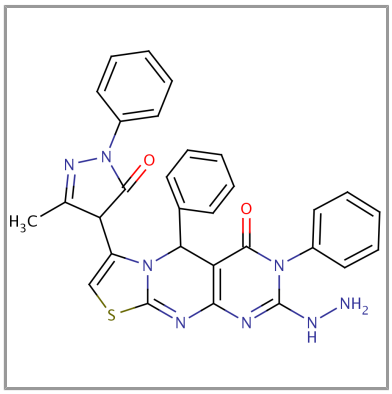

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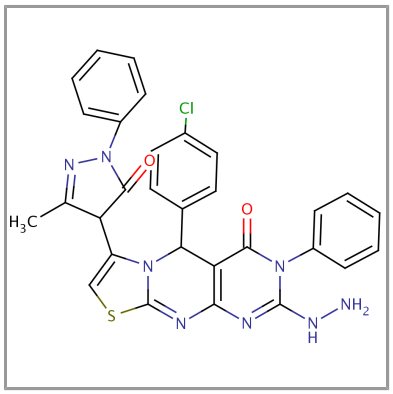

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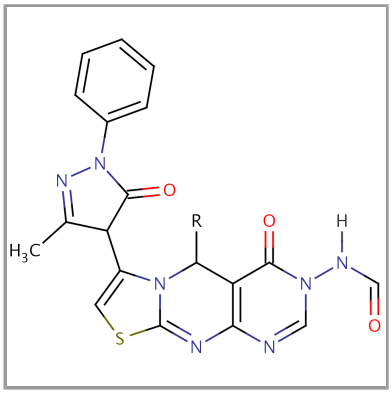

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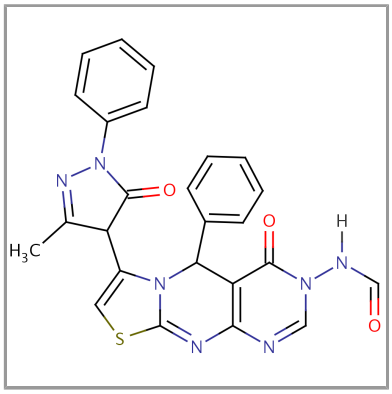

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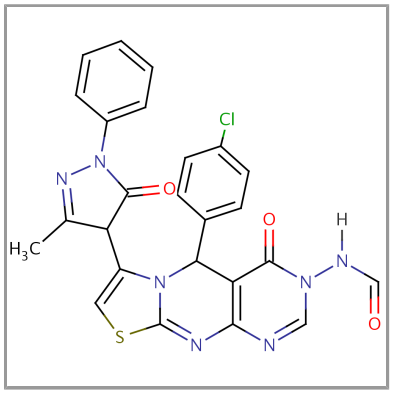

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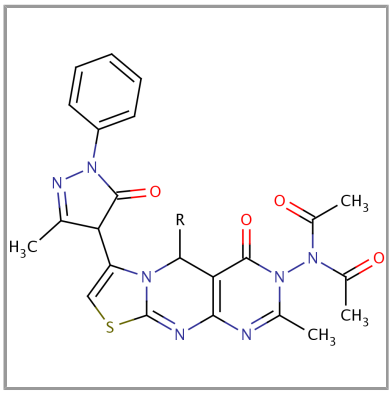

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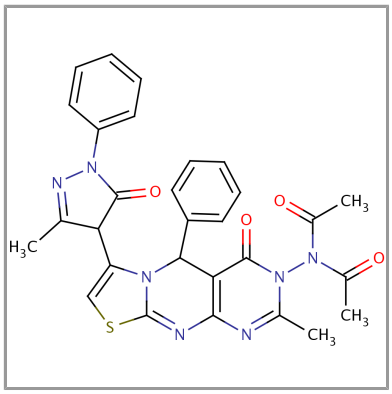

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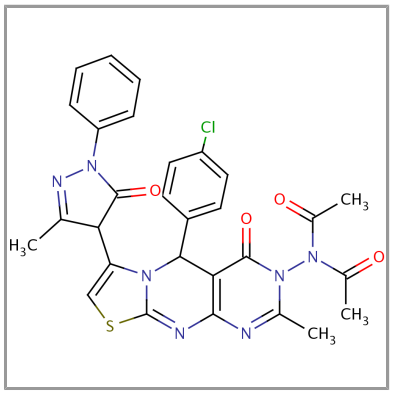

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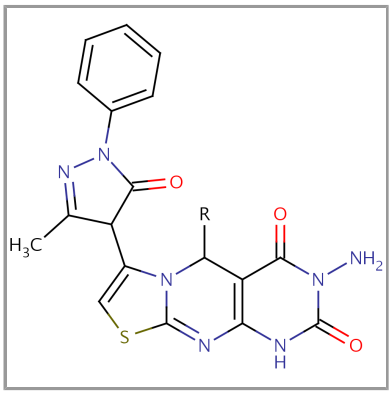
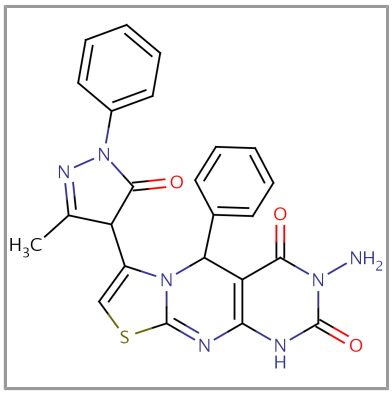


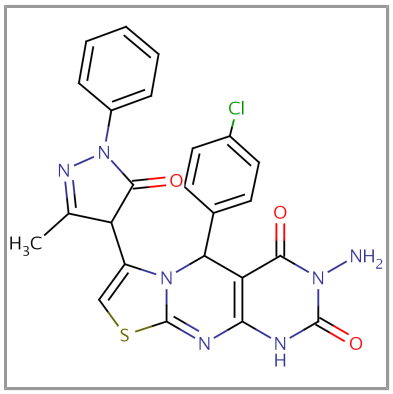
Compound Details Structure Search

10a



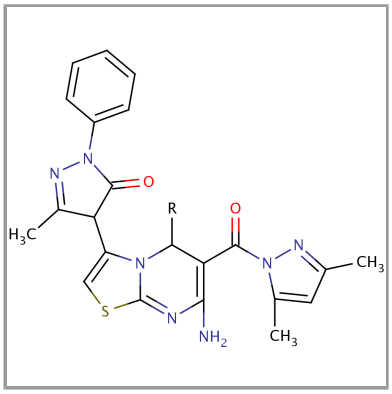
Compound Details Structure Search

10b



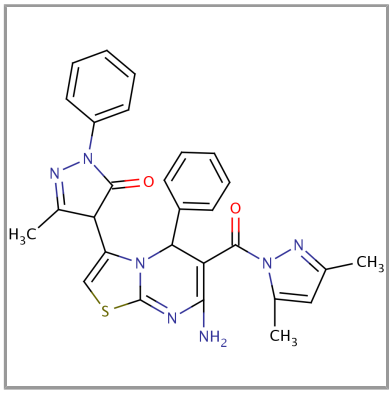
Compound Details Structure Search

11



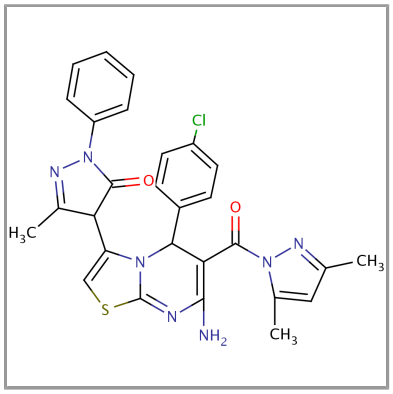
Compound Details Structure Search

11a



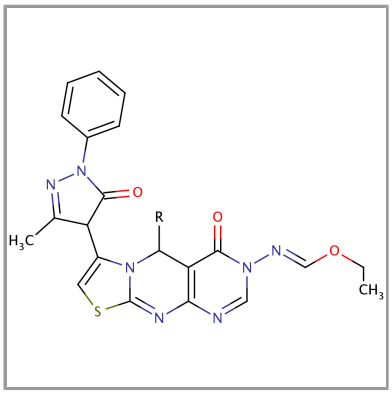
Compound Details Structure Search

11b



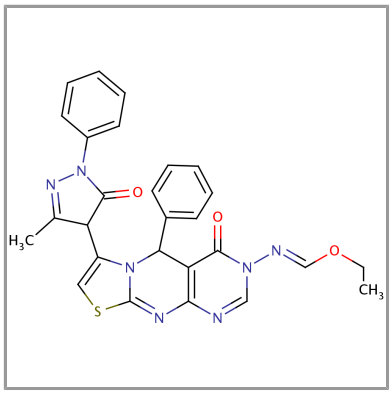
Compound Details Structure Search

12



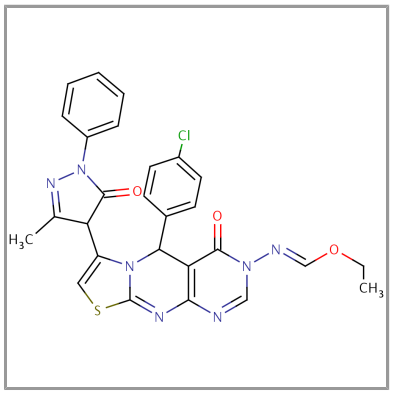
Compound Details Structure Search

12a



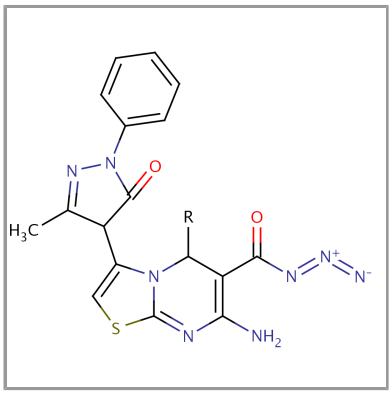
Compound Details Structure Search

12b



Compound Details Structure Search

13



Compound Details Structure Search

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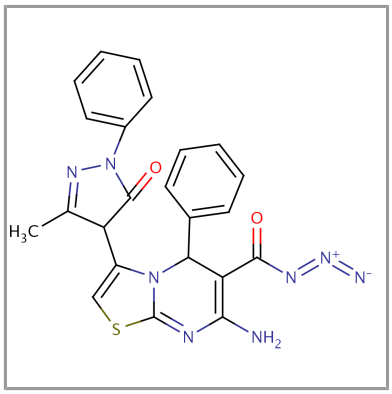
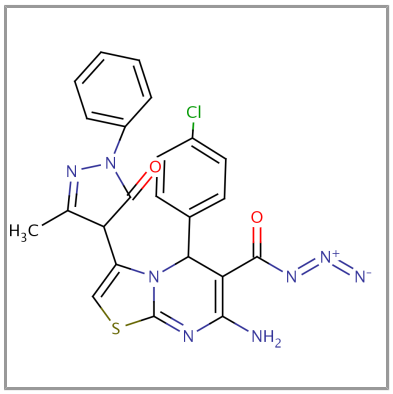


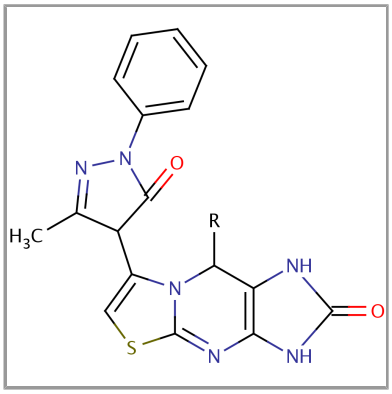
Compound Details Structure Search

13b



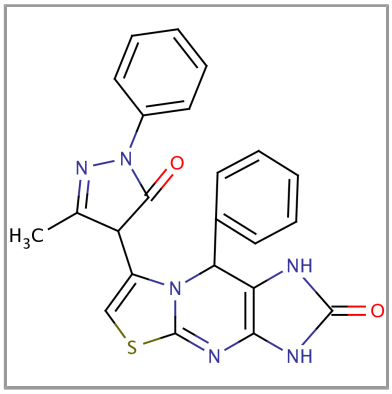
Compound Details Structure Search

14



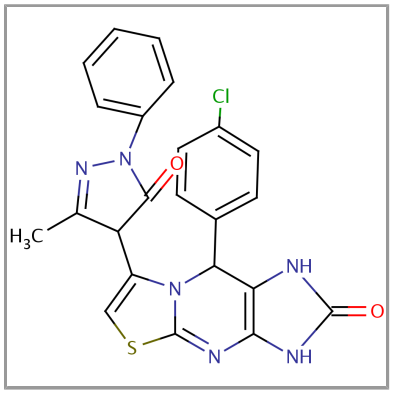
Compound Details Structure Search

14a



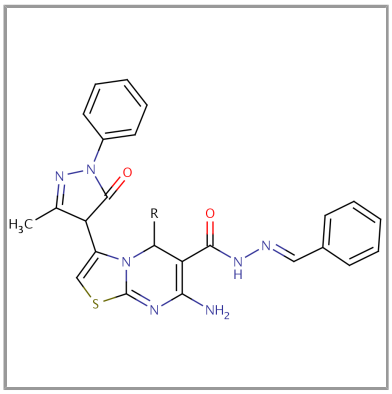
Compound Details Structure Search

14b



Compound Details Structure Search

15



Compound Details Structure Search

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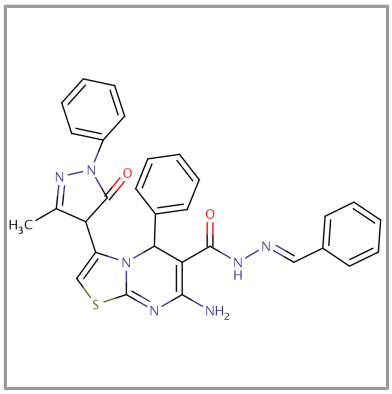
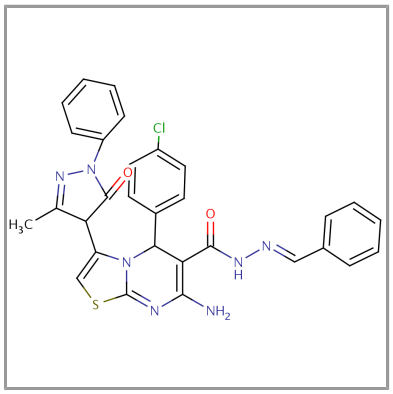


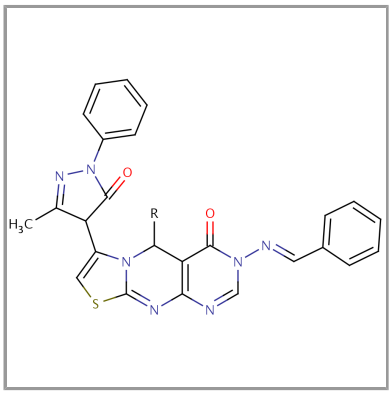
Compound Details Structure Search

15b



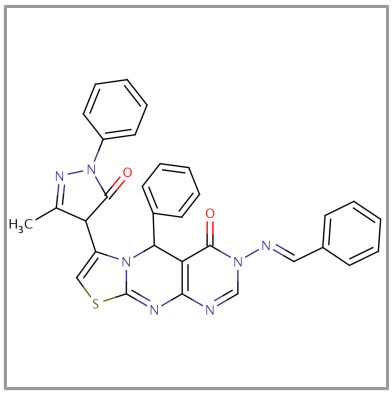
Compound Details Structure Search

16



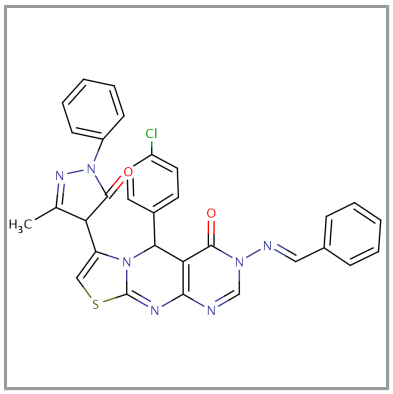
Compound Details Structure Search

16a



Compound Details Structure Search

16b



Compound Details Structure Search