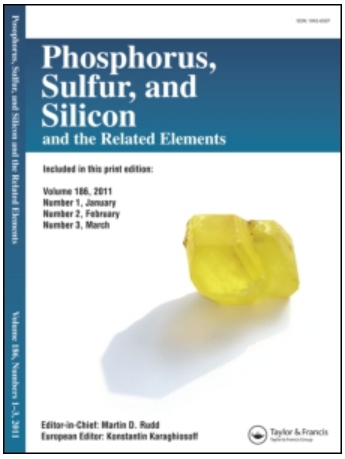

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NEW PYRIMIDINE DERIVATIVES: SYNTHESIS AND APPLICATION OF THIAZOLO[3,2-a]-TRIAZOLO[4,3-a]-PYRIMIDINE AS BACTERICIDES, FUNGICIDES AND BIOREGULATORS

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NEW PYRIMIDINE DERIVATIVES: SYNTHESIS AND APPLICATION OF THIAZOLO[3,2-a]-TRIAZOLO[4,3-a]-PYRIMIDINE AS BACTERICIDES, FUNGICIDES AND BIOREGULATORS

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5-Cyano-4-oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydro pyrimidine[1] (**I**) reacts with alkyl or alkaryl halides to give the corresponding 2-alkyl (alkaryl) derivatives (**IIa–g**); and with chloroacetic acid ethyl chloroacetate to give compounds **III** and **IV** respectively further reaction of **IV** with ammonia and amines yielded 5-cyano-2(glycolamidethio)-6-phenyl pyrimidine-4(3H) one derivatives (**Va–g**). The parent thiazolo[3,2-a]pyrimidine (**VI**) was prepared from compound **III** by refluxing with acetic anhydride. Also compound I reacted with hydrazine hydrate to give 2-hydrazino derivative **IX** was converted into a variety of triazolo[4,3-a] pyrimidine derivatives. The biological activity of the new compounds was tested as microbicidal and bioregulator agents, the results obtained were correlated with their structure.

Key words: Pyrimidinethione; thiazolopyrimidine; triazolopyrimidine; synthesis and reactions; biological activity.

INTRODUCTION

Pyrimidine and its derivatives constitute a number of nucleic acid bases such as cytosine, thymine, uracil, adenine etc. The nucleic acid bases carry the genetic information required for the synthesis of different proteins and enzymes.[2] Also it seemed to be the possible target for the action of many drugs either directly or indirectly by induction or inhibition of protein synthesis and other biochemical processes.[3]

Pyrimidine fused heterocycles occupy a position of unique significance in medicinal chemistry. Azolopyrimidines for example have considerable biological and medicinal activities as: vasodialators anticholester emics and in blood platelet aggregation.[4]

Within this respect, the present work is aimed to synthesise uninuclear cyanopyrimidine derivatives or compounds fused with other azolo heterocyclic ring systems to study their possible biological activities as antimicrobial and as bioregulator agents. Structure activity relationships has also been studied to detect the preferable structures required for such purposes.

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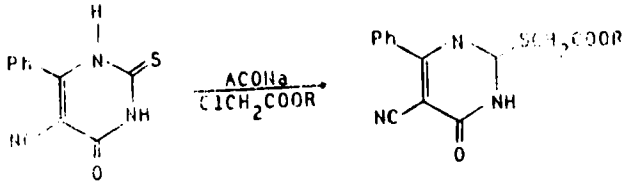
Our approach to the synthesis of the desired pyrimidines started with 5-cyano-4-oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydro pyrimidine[1] (**I**).

RESULTS AND DISCUSSION

2-Alkyl (alkaryl) thio derivatives (**IIa–g**) were synthesised by refluxing of (**I**) with alkyl (alkaryl) halide in ethanol containing fused sodium acetate as a basic catalyst. The results are given in Table I.

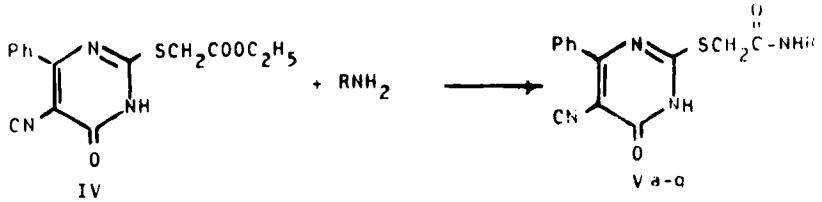
Interaction of **I** with chloroacetic acid and/or ethyl chloroacetate in ethanol containing anhydrous sodium acetate gives the corresponding 5-cyano-2(glycolic acid thio)-6-phenyl pyrimidine 4(3H) one (**III**) and its ester derivative (**IV**) respectively. The reaction is represented as follows:



I

III, R=H
IV, R=Et

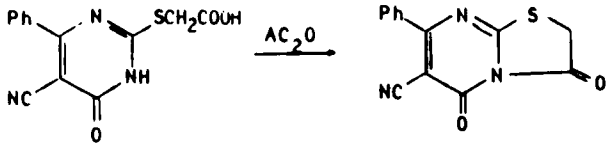
The reaction of (**IV**) with ammonia-, aliphatic, aromatic-, and heterocyclic amines in ethanol gives the substituted amide derivatives 5-cyano-2(glycolamid thio)-6-phenyl pyrimidine 4(**3H**) ones (**Va–g**) (c.f. Table II).



IV

Va-g

The thiazolo[3,2-a]pyrimidine-3,5-dione derivative (VI) was prepared by refluxing compound (III) in redistilled acetic anhydride.



III VI

The thiazolo[3,2-a]pyrimidine derivative (**VIII**) was prepared by the reaction of (**I**) with 3-chloropentan-2,4-dione in presence of KOH to give the intermediate

TABLE I

Physical and analytical data of 2-alkyl (alkaryl [R]) thio-5-cyano-6-phenylpyrimidine-4(3H)-ones (**IIa–g**)

Compd.	R	mp. °C	Yield %	R_F* Value	Moleclar formula	Analytical data Calcd./(Found (%) C	H	N	S
IIa	CH_3	284	76	0.52	$C_{12}H_9N_3OS$	59.25	3.70	17.28	13.16
						58.89	3.44	17.10	12.91
b	C_2H_5	246	65	0.41	$C_{13}H_{11}N_3OS$	60.70	4.28	16.34	12.45
						61.03	4.53	16.16	12.30
c	C_3H_7(iso)	225	60	0.54	$C_{14}H_{13}N_3OS$	61.99	4.79	15.49	11.80
						61.69	5.16	15.30	12.21
d	C_4H_9(2)	191	62	0.63	$C_{15}H_{15}N_3OS$	63.15	5.26	14.73	11.22
						63.41	4.93	14.39	11.43
e	C_4H_9(n)	182	71	0.39	$C_{15}H_{15}N_3OS$	63.15	5.26	14.75	11.22
						62.94	5.11	14.52	10.88
f	C_5H_{11}	170	68	0.40	$C_{15}H_{17}N_3OS$	64.21	5.68	14.04	10.70
						64.53	5.46	13.89	10.55
g	$CH_2C_6H_5$	203	52	0.37	$C_{18}H_{13}N_3OS$	67.71	4.07	13.16	10.03
						67.44	3.87	13.37	9.82

* Eluent: Acetone-Pet. ether (3–7).

TABLE II

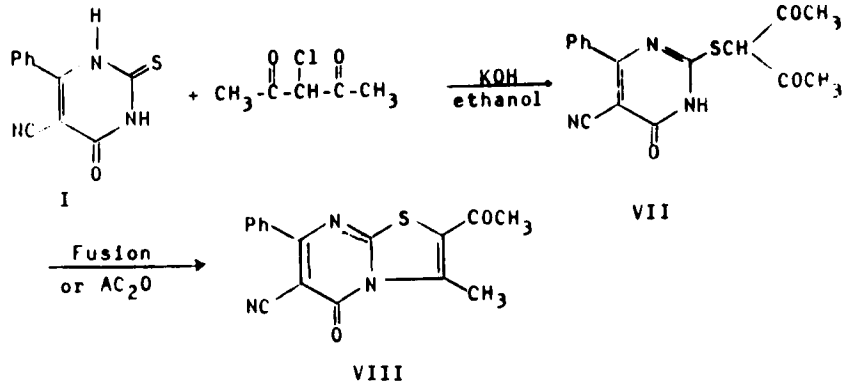
Physical and analytical data of 5-cyano-2-(glycolamide thio)-6-phenylpyrimidin-4(3H)-one and its substituted amide (**Va–g**)

Compd.	Ar.	mp. °C	Yield %	R_F* Value	Molecular formula	Analytical data Calcd./Found (%) C	H	N	S	Cl
Va	H	243	70	0.59	$C_{13}H_{10}N_4O_2S$	54.54	3.49	19.58	11.18	—
						54.23	3.27	19.41	11.31	—
b	C_2H_5	234	73	0.53	$C_{15}H_{14}N_4O_2S$	57.32	4.45	17.83	10.19	—
						57.56	4.32	17.98	10.62	—
c	C_4H_9	223	67	0.57	$C_{17}H_{18}N_4O_2S$	59.64	5.26	16.37	9.35	—
						59.60	5.11	16.23	9.30	—
d	C_6H_5	330	63	0.39	$C_{19}H_{14}N_4O_2S$	62.98	3.86	15.46	8.83	
						62.76	3.76	15.63	8.76	—
e	C_6H_4Cl (p)	348	72	0.30	$C_{19}H_{13}N_4O_2SCl$	57.50	3.27	14.12	8.07	8.95
						57.33	3.45	14.33	8.26	8.72
f	2-pyridyl	187	60	0.61	$C_{18}H_{13}N_5O_2S$	59.50	3.58	19.28	8.81	
						59.24	3.71	19.07	9.03	
g	3-pyridyl	358	52	0.42	$C_{18}H_{13}N_5O_2S$	59.50	3.58	19.28	8.81	
						59.36	3.65	19.42	8.67	

* Acetone-Pet. ether (2.8).

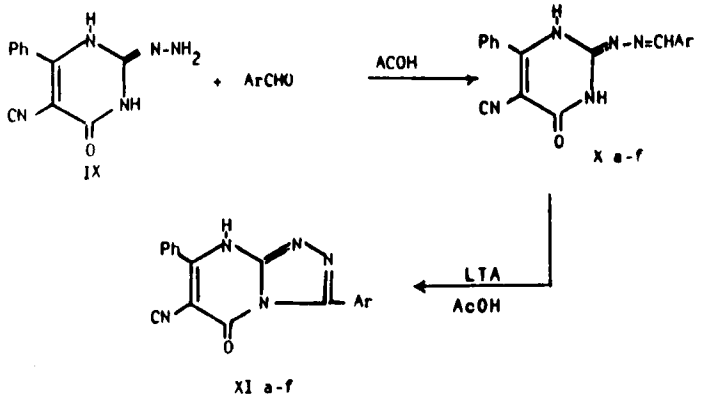
(**VII**) which underwent cyclisation by fusion above its melting or by heating in redistilled acetic anhydride.

Compound (**I**) reacts with hydrazine hydrate in ethanol to give 5-cyano-2-hydrazono-6-phenyl-1,2,3,4-tetrahydro pyrimidin-4-one(**IX**). Further reaction of compound **IX** with aromatic aldehydes in acetic acid give the corresponding azines (**Xa–f**), which underwent cyclodehydrogenation to form 3-aryl-6-cyano-7-



I VII VIII

phenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(**8H**) ones (**XIa–f**) (Tables III & IV).



IX X a-f XI a-f

The fused triazolo[4,3-a]pyrimidine derivatives (**XIII**, **XV**, **XVI**, **XVII**) were achieved via interaction of compound (**IX**) with acetic anhydride, formic acid

TABLE III

Physical and analytical data of 2-arylidenehydrazono-5-cyano-6-phenyl-1,2,3,4-tetrahydropyrimidine-4-ones (**Xa–f**)

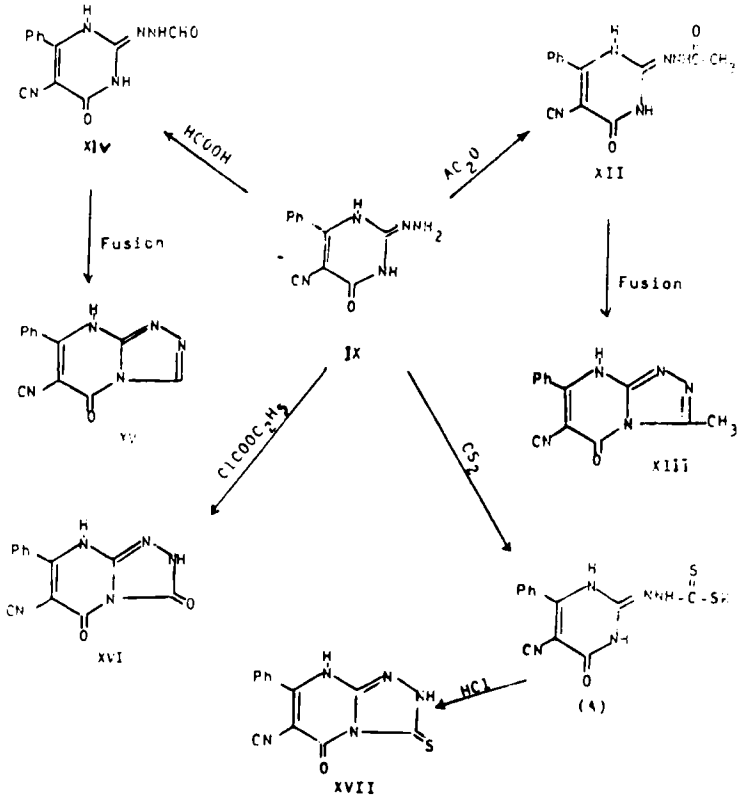
Compd.	Ar.	mp. °C	Yield %	Molecular formula	Analytical data Calcd./Found C	H	N	Cl
Xa	C_6H_5	311	75	$C_{18}H_{13}N_5O$	68.57	2.12	22.22	—
					68.10	4.10	22.34	—
b	C_6H_4-NO (p)	320	86	$C_{18}H_{12}N_6O_3$	60.0	3.33	23.33	—
					60.32	3.11	23.10	—
c	C_6H_4-Cl(p)	298	82	$C_{18}H_{12}N_5OCl$	61.80	3.43	20.02	10.15
					61.56	3.16	20.30	9.95
d	C_6H_4-OH(o)	309	65	$C_{18}H_{13}N_5O_2$	65.25	3.92	21.14	—
					65.03	3.78	21.25	—
e	C_6H_4-OCH_3(p)	316	80	$C_{19}H_{15}N_5O_2$	66.08	4.34	20.28	—
					66.24	4.56	20.05	—
f	$C_6H_4N(CH_3)_2$(p)	304	63	$C_{20}H_{18}N_6O$	67.03	5.02	23.46	—
					67.25	5.19	23.33	

TABLE IV

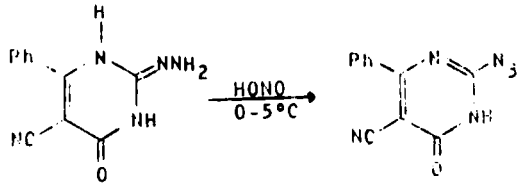
Physical and analytical data of 3-aryl-6-cyano-7-phenyl[1,2,4]triazolo[4,3-a]-pyrimidin-5(8H) ones (**XIa–f**)

Compd.	Ar	mp.°C solvent	Yield %	Molecular formula	Analytical data Calcd./Found C	H	N	Cl
XIa	$-C_6H_5$	235 Ethanol	65	$C_{18}H_{11}ON_5$	69.00 68.87	3.51 3.35	22.36 22.62	— —
b	C_6H_4-$NO_2(p)$	295 Ethanol	80	$C_{18}H_{10}O_3N_6$	60.33 60.62	2.79 2.63	23.46 23.25	— —
c	C_6H_4-$Cl(p)$	275 Benzene	76	$C_{18}H_{10}ON_5Cl$	62.95 62.37	2.87 2.98	20.14 20.39	10.21 10.43
d	C_6H_4-$OH(o)$	262 Acetic acid	60	$C_{18}H_{11}O_2N_5$	65.65 65.47	3.34 3.11	21.27 21.16	— —
e	C_6H_4-$OCH_3(p)$	330 Ethanol	73	$C_{19}H_{13}O_2N_5$	66.47 66.56	3.79 3.53	20.40 20.31	— —
f	C_6H_4-$N(CH_3)_2(p)$	249 Ethanol	57	$C_{20}H_{16}ON_6$	67.41 67.65	4.49 4.65	23.59 23.32	— —

ethyl chloroformate and carbon disulphide.

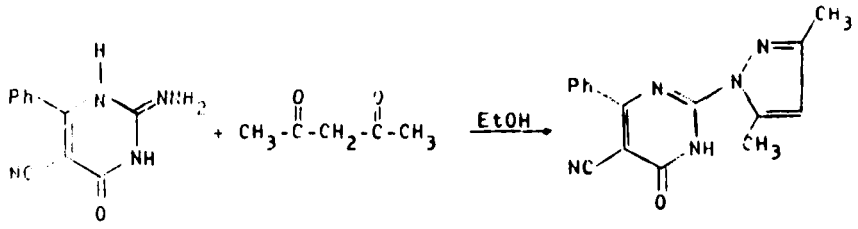


2-Azido-5-cyano-6-phenyl pyrimidin-4(**3H**) one (**XVIII**) was obtained by the action of nitrous acid on (**IX**).



IX XVIII

5-Cyano-2(3,5-dimethyl-1-pyrazolyl)-6-phenyl pyrimidin-4(**3H**) one (XIX) was synthesized by interaction of hydrazono compound (IX) and acetyl acetone in ethanol.



IX XIX

The structure of the prepared compounds was elucidated on the basis of elemental analysis as well as spectral data.

Structure activity relationships is quite clear among the studied compounds as follows:

2-Substituted thiopyrimidines and 2-iminopyrimidine derivatives:

Compound **I** is effective against *Micrococcus luteus* and *Pseudomonas aeruginosa* (45 mm). Substitution of the C=S group by an alkylthio group (Table V) largely affects its activity and this effect is quite dependent on the length and branching of the alkyl side chain. It is increased by increasing the length of the *n*-alkyl side chain and is destroyed by branching. In case of **IIf** the activity is extended towards *Bacillus cereus, Serratia sp.* besides *P. aeruginosa.* Substitution by benzyl group **IIg** increased its activity by 2 fold (80 mm relative to 40 mm for —SMe) and extended the performance only towards *serratia sp.* substitution of 2-thioxo group by thioglycolic acid (Table VI) destroyed its activity. Esterification of the —COOH group induced strong bactericidal activity against *P. aeruginosa*

TABLE V

Comp.	*Micrococcus luteus*	*Bacillus cereus*	*Serratia sp.*	*Pseudomonas aeruginosa*	*Penicillium duclauxi*	*Aspergillus flavus*	*Stachybotrys atra*
I	25	-ve	-ve	45	-ve	16	20
IIa	-ve	-ve	-ve	40	-ve	-ve	-ve
IIb	-ve	-ve	-ve	50	-ve	20	-ve
IIc	-ve	-ve	-ve	-ve	-ve	-ve	17
IId	-ve	-ve	-ve	-ve	-ve	-ve	20
IIe	-ve	-ve	-ve	60	-ve	25	18
IIf	-ve	15	17	55	-ve	-ve	23
IIg	-ve	-ve	30	80	-ve	10	18

TABLE VI

Comp.	*Micrococcus luteus*	*Bacillus cereus*	*Serratia sp.*	*Pseudomonas aeruginosa*	*Penicillium duclauxi*	*Aspergillus flavus*	*Stachybotrys atra*
III	-ve	-ve	-ve	-ve	-ve	20	-ve
IV	45	-ve	-ve	85	-ve	13	-ve
Va	-ve	-ve	-ve	85	18	-ve	-ve
Vb	-ve	-ve	-ve	85	16	38	-ve
Vc	-ve	20	-ve	85	-ve	60	-ve
Vd	-ve	20	-ve	85	-ve	-ve	16
Ve	-ve	-ve	-ve	50	-ve	-ve	-ve
Vf	-ve	-ve	-ve	35	ve	25	-ve
Vg	-ve	-ve	-ve	-ve	ve	-ve	-ve

(85 mm) and moderate activity against *M. luteus* (45 mm). The amide derivative Va is highly active against *P. aeruginosa,* with bluish violet color, while substitution of the amide as in **Vb–d** give no color with any of the microorganisms tested. Further substitution at the phenyl ring decreased its activity. Replacement of the phenyl moiety by a heterocyclic pyridine nucleus affected the activity which depended on linkage position. Activity was decreased to half in case of 2-pyridy (**Vf**) and has no effect for 3-pyridyl (**Vg**). Substitution of the thioxo group in **I** by hydrazono **IX** (Table VII) showed strong activity against *P. aeruginosa* (85 mm), while substitution by arylimino or azide group XVIII destroyed its activity. Replacement of the thioxo group by pyrozole ring **XIX** sharply decreased its effect and exhibited minor activity against *M. luteus.*

Effect of fused pyrimidine heterocycls (triazolo[4,3-a]-, thiazolo[3,2-a]pyrimidines):

The parent triazolo pyrimidine derivative (**XV**) is quite active against *P. aeruginosa* (85 mm) and inactive against other microorganisms. Substitution of 3-hydrogen atom by other groups decreased its activity. Phenyl triazolo-pyrimidine **XIa** showed less activity than its methyl derivative XIII. Further substitution by electron donating group (e.g. OMe) at the phenyl ring **XIe** slightly enhanced its activity, while electron withdrawing groups (e.g. NO_2 **XIb**) destroyed it.

Substitution by an oxo group **XVI** destroyed its activity, while the thioxo XVII restored its bactericadal activity by less than one half. Compound **VI** possessed bactericidal activity against *M. luteus, serratia sp.* and *P. aeruginosa,* while **VIII** showed strong activity against *P. aeruginosa* only.

As fungicides: Compound **I** possessed fungicidal activity against *Aspergillus flavus* and *Stachybotrys atra* (16 mm and 20 mm respectively). Substitution of

TABLE VII

Comp.	*Micrococcus luteus*	*Bacillus cereus*	*Serratia sp.*	*Pseudomonas aeruginosa*	*Penicillium duclauxi*	*Aspergillus flavus*	*Stachybotrys atra*
X	-ve	-ve	-ve	85	-ve	-ve	-ve
IXa	-ve	-ve	-ve	-ve	-ve	-ve	-ve
XIX	-ve	-ve	-ve	-ve	-ve	15	-ve
XXII	17	-ve	-ve	-ve	-ve	-ve	20

thioxo group in **I** with methyl thio derivative **IIa** destroyed its fungicidal activity, while increasing the alkyl side chain length restored it. Substitution by thioglycolic acid slightly enhanced the activity against *A. flavus* only. The fused triazolopyrimidine is inactive, however, its methyl derivative **XIII** showed minor activity against *S. atra* only. Replacement of the methyl by phenyl group in XIa extended its activity towards *A. flavus*. Activity against *S. atra* was decreased at XIe and completely destroyed at **XIb**.

For Higher organism: Compound **III** and **XV** enhanced the growth of seedlings, while alkylthio derivatives **IIa–g** retarded it, which suggest the use of the former as plant growth promotors and the later as plant growth inhibitor. The other derivatives had a minor effect on the germenation at this concentration (Table IX). The estimation of both, growth promotor for the thioglycolic acid derivative **III**, triazolopyimidine **XV** and growth inhibitor for **IIIe** is given in Table VIII and Figure 1.

TABLE VIII

Effect of heterocyclic compounds incorporating cyanophenylpyrimidine moiety on germination of *Vicia faba* seeds (20 seeds) after 14 days of planting

No.	Compound	No. of germinated seeds	Average of shoot length relative to		Root length cm
			20 seeds	germinated seeds	
	Control	19	16.35	17.00	18
I	—SH	14	9.10	13.00	16.25
IIa	—S—CH_3	16	8.00	10.00	15.25
IIb	—S—C_2H_5	17	9.60	11.29	14.28
IIc	—S—$CH(CH_3)_2$	19	12.00	12.80	21.00
IId	—S—$CH(CH_3)CH_2CH_3$	17	8.40	9.90	16.00
IIe	—S—$CH_2CH_2CH_2CH_3$	14	6.20	8.70	8.50
IIf	—S—$CH_2CH_2CH_2CH_2CH_3$	17	8.15	9.60	12.56
IIg	—S—CH_2Ph	18	7.00	7.90	14.25
III	—S—CH_2COOH	20	18.50	18.50	20.50
IV	—S—CH_2COOEt	20	13.60	13.60	19.75
Va	—S—$CH_2\overset{\overset{O}{\|}}{C}NH_2$	19	14.30	15.05	17.25
Vb	—S—$CH_2CONHEt$	19	14.95	15.80	18.75
Vc	—S—$CH_2CONHBu$	20	13.70	13.70	20.75
Vd	—S—$CH_2\overset{\overset{O}{\|}}{C}NHPh$	18	15.15	16.80	17.25
Vf	—S—$CH_2\overset{\overset{O}{\|}}{C}$—NH—$C_5H_4N(2)$	20	14.50	14.50	17.75
Vg	—S—$CH_2\overset{\overset{O}{\|}}{C}$—NH—$C_5H_4N(3)$	20	16.00	16.00	19.00
IX	2-Phenylimino	18	11.40	12.66	14.25
X	2-Hydrazono	18	9.65	10.60	12.00
XXII	2-pyrazolyl	19	10.70	11.26	18.75
XVI	Triazolpyrimidine	20	17.10	17.10	22.00
IVIII	Triazolthione	20	14.20	14.20	17.00
VIII	Acetylthiazolo	20	15.75	15.75	17.75

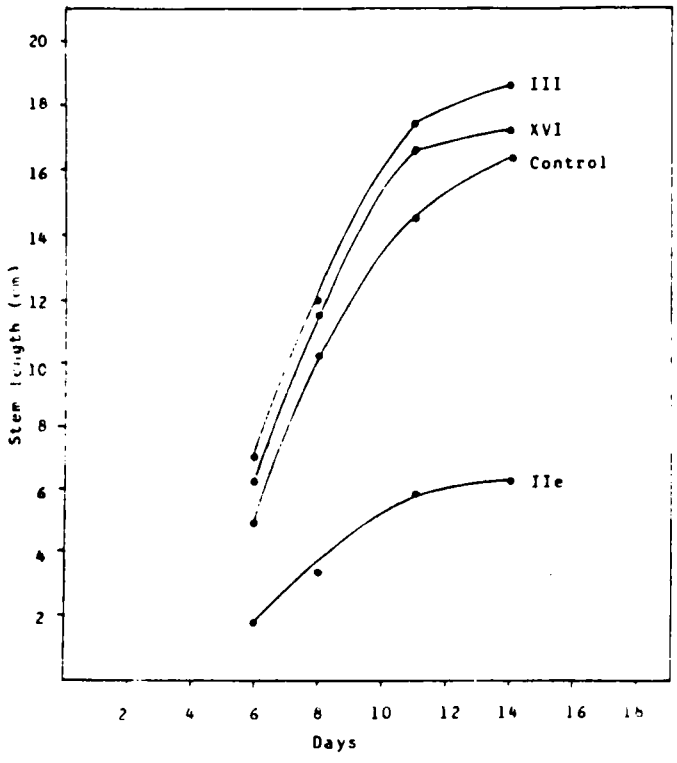


FIGURE 1.

TABLE IX

Rate of shoot growth of *Vicia faba* seeds after treatment by pyrimidine derivatives at 100 ppm

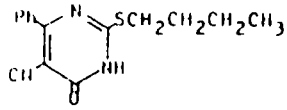
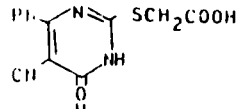
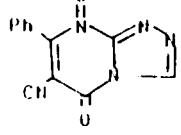
No.	Compound	No. of germinated seeds	Average of shoot length relative to 20 seeds after			
			6 days	8 days	11 days	14 days
	Control	19	4.9	10.25	15.50	16.25
IIe						
III		14	1.8	3.35	5.65	6.20
XVI		20	7.0	12.00	17.35	18.50
		20	6.2	11.60	16.60	17.10

TABLE X

Effect of different concentrations of (III) on the germination rate of *Vicia faba* seeds

Concentration	No. of germinated seeds	Average of shoot length relative to 20 secs after				Average of root length after 14 days
		6 days	8 days	11 days	14 days	
Control (zero)	20	2.40	3.05	4.60	6.15	9
2 ppm	18	2.70	4.15	5.10	7.50	13
5 ppm	18	3.75	6.05	7.60	11.50	16
10 ppm	20	3.45	5.65	8.00	11.10	22
20 ppm	17	3.55	6.00	7.50	10.40	19
50 ppm	19	3.80	7.60	9.20	12.95	23
100 ppm	19	6.15	10.05	12.10	14.90	20
250 ppm	18	4.50	7.70	8.10	11.35	20
500 ppm	19	3.20	5.45	5.85	8.45	14
1000 ppm	15	2.40	4.25	5.80	8.30	16
2000 ppm	19	2.25	3.80	4.10	5.75	14

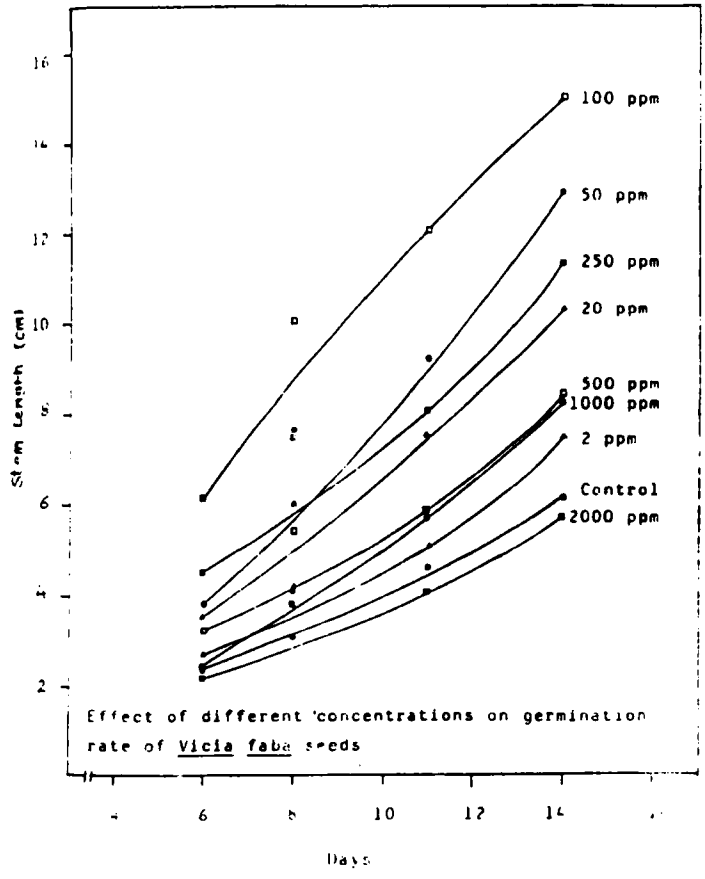


FIGURE 2.

The effect of concentration of the more effective compound **III** on the germination of *vicia faba* seeds is studied. The results obtained are summarized in Table XI and Figure 2. It is clear that the rate of germination (relative to the control) increased progressively with increase of the concentration to reach a maximum at 100 ppm. The opposite occurred at concentration higher than 100 ppm with a minimum at 2000 ppm. Also, any treatment with the substance effected not only the shoot length but also the root length.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded in potassium bromide on a Perkin–Elmer spectrophotometer. The ^{1}H nmr spectra were recorded in DMSO-d_6 on a Varian 90 MHZ using TMS as internal standard (Chemical shifts in δppm).

1-Preparation of 2-alkyl (alkaryl) thio-5-cyano-6-phenyl pyrimidin-4(3H) ones **IIa–g**. A mixture of (I) (0.01 mol), alkyl, (alkaryl) halide (0.01 mol) and anhydrous ACONa (2 g) was refluxed in ethanol (20 ml) for about 2 hours, then cooled, and acidified with dilute hydrochloric acid. The precipitated product was filtered off and recrystallised from ethanol.

2-Preparation of 5-cyano-2-(glycolic acid thio)-6-phenyl pyrimidin-4(3H) one (III) and its ester derivative (**IV**). A mixture of (I) (0.01 mol), chloroacetic acid (ethyl chloro acetate) and anhydrous ACONa (2 gm) was refluxed in ethanol (30 ml) for about 5 hours. The reaction mixture was cooled, acidified with dilute hydrochloric acid, the precipitate was filtered off and recrystallised from ethanol.

Compound **III** formed white crystals m.p. 22°C yield 2.2 g. i.r: 3190 (NH), 2500–2700 (OH carboxyl), 2215 (C≡N), 1720 (C=O acid) and 1655 cm^{-1} (C=O pyrimidinone).

Anal Calcd.: $C_{13}H_9N_3O_3S$: C, 54.35; H, 3.13; N, 14.63; S, 11.14%.
Found: C, 54.10; H, 2.99; N, 14.75; S, 10.83%.

Compound **IV** formed pale yellow crystals m.p. 250°C yield 2.3 g. i.r.: 3180 (NH), 2215 (CN), 1730 (C=O ester) and 1660 cm^{-1} (C=O pyrimidinone).

Anal. Calcd.: $C_{15}H_{13}N_3O_3S$: C, 57.14; H, 4.12; N, 13.33; S, 10.15%.
Found: C, 57.44; H, 4.33; N, 12.98; S, 10.18%.

3-Preparation of 5-cyano-2-(glycolamide thio)-6-phenylpyrimidin-4(3H) one and its substituted amides (**Va–g**). A mixture of (IV) (0.01 mol) and ammonia, aliphatic-, aromatic- or heterocyclic amines (0.01 mol) was refluxed in ethanol (25 ml) for about 2 hours. The reaction mixture was cooled, the precipitated products were filtered off and recrystallised from ethanol.

4-Preparation of 6-cyano-2,3-dihydro-7-phenyl thiazolo[3,2-a]-pyrimidin-3,5-dione (**VI**). Compound (III) (0.01 mol) was refluxed with acetic anhydride (10 ml) for 2 hours. The reaction mixture was cooled, the precipitate was collected and recrystallised from acetic acid to give straw colour crystals of (VI) m.p. 357°C, yield 1.9 g. i.r. 2210 (CN), 1780 (C=O thiazolidinone) and 1680 cm^{-1} (C=O pyrimidinone), ^{1}H NMR δ 7.6 (m, SH, arom) and δ 2.8 (s, 2H, CH_2).

Anal Calcd.: $C_{13}H_7N_3O_2S$: C, 57.99; H, 2.6; N, 15.61; S, 11.89%.
Found: C, 58.4; H, 2.67; N, 15.51; S, 11.47%.

5-Preparation of 5-cyano-2-(3-pentan-2,4-dione thio)-6-phenyl pyrimidine-4(3H) one (**VII**). A mixture of (I) (0.01 mol) and KOH (0.012 mol) in ethanol (30 ml) was stirred for 5 minutes, then 3-chloropentan 2,4-dione (0.01 mol) was added dropwise while stirring. The precipitate was filtered off and recrystallised from acetic acid to give pale yellow crystals of (VII), m.p. 238°C yield 2.4 g. i.r.: 3130 (NH), 2210 (C≡N) 1670 (2C=O -diketone) an 1650 cm^{-1} (C=O pyrimidinone).

6-Preparation of 2-acetyl-6-cyano-3-methyl-7-phenyl thiazolo[3,2-a]pyrimidin-5-one (**VIII**). Compound (VII) (0.01 mol) was fused above its melting point at ~250°C on heating mantel for about one hour. The product was triturated with ethanol, filtered off and recrystallised from acetic acid to give orange crystals of (VIII) m.p. 212°C yield 1.7 g i.r.: 2200 (C≡N), 1700 (C=O acetyl) and 1660 cm^{-1} (C=O pyrimidinone), ^{1}H NMR δ7.5 (m, 5H arom), δ3.2 (s, 3H acetyl) and δ2.65 (s, 3H methyl).

7-Preparation of 5-cyano-2-hydrazono-6-phenyl-1,2,3,4-tetrahydro pyrimidin-4-one (**IX**). A mixture

of (I) (0.01 mol) and hydrazine hydrate (0.02 mol) was fused till ceasing of hydrogen sulphide gas, followed by refluxing the reaction mixture in ethanol for about 4 hours. The precipitated product was filtered off and recrystallised from acetic acid into pale yellow crystals of (IX) m.p. 244°C yield 1.7 g. i.r.: 3290 (NH_2), 3110, 3090 (NH), 2210 (C≡N) and 1690 cm^{-1} (C=O pyrimidinone).

Anal. Calcd.: $C_{11}H_9NSO$: C, 58.14; H, 3.96; N, 30.83%.
Found: C, 58.51; H, 4.20; N, 30.63%.

8-Preparation of 2-arylidene hydrazono-5-cyano-6-phenyl-1,2,3,4-tetrahydro pyrimidin-4-ones (**Xa–f**). A mixture of (IX) (0.01 mol) and aromatic aldehyde (0.01 mole) was refluxed in acetic acid (20 ml) for about one hour. The precipitated product was filtered off and recrystallised from acetic acid.

9-Preparation of 3-aryl-6-cyano-7-phenyl[1,2,4[triozol[4,3-a]-pyrimidin-5-(8H) ones (**XIa–f**). A mixture of (**XIa–f**) (0.01 mol) and lead tetra acetate (0.01 mol) was refluxed in acetic acid (20 ml) for about 3 hours. The reaction mixture was cooled and poured onto cold water. The precipitated product was filtered off and recrystallised from the proper solvent.

10-Preparation of 5-cyano-2-(N-acetyl hydrazono)-6-phenyl-1,2,3,4-tetrahydro pyrimidin-4-one (**XII**). A mixture of (IX) (0.01 mol) and acetic anhydride (10 ml) was refluxed for about 3 hours, then poured onto cold water. The separated product was filtered off and recrystallised from acetic acid to give white crystals of (XII) m.p. 210 yield 2 g, i.r.: 3450, 3400 (NH), 2200 (C≡N), 1750 (C=O amide) and 1670 cm^{-1} (C=O pyrimidinone).

Anal. Calcd.: $C_{13}H_{11}N_5O_2$; C, 57.99; H, 4.08; N, 26.02%.
Found: C, 57.67; H, 4.23; N, 26.13%.

11-Preparation of 6-cyano-3-methyl-7-phenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(8H) one (**XIII**). Compound (**XII**) (0.01 mol) was fused above its melting point at ≈220°C for about one hour. The solidified product was triturated with ethanol, filtered off and recrystallised from absolute ethanol to give lustrous crystals of (**XIII**) m.p. 320°C yield 1.6 g. i.r.: 3130 (NH), 2210 (C≡N) and 1660 cm^{-1} (C=O pyrimidinone). ^1H NMR δ 7.6 (m, 5H arom), δ 4.3 (s, 1H, NH) and δ 2.6 (s, 3H, CH_3).

Anal. Calcd.: $C_{13}H_{19}N_5O$: C, 62.15; H, 3.58; N, 27.88%.
Found: C, 62.89; H, 3.27; N, 27.95%.

12-Preparation of 5-cyano-2-(N-formyl hydrazono)-6-phenyl-1,2,3,4-tetrahydro pyrimidin-4-one (**XIV**). A mixture of (**IX**) (0.01 mol) and formic acid (5 ml) was refluxed for 3 hours in ethanol (30 ml). The precipitated product was filtered off and recrystallised from ethanol to give yellowish white crystals of (XIV) m.p. 243°C, yield 1.8 g, i.r.: 3450, 3130 3100 (NH), 2200 (C≡N), 1700 (C=O formyl) and 1670 cm^{-1} (C=O pyrimidinone).

Anal. Calcd.: $C_{12}H_9N_5O_2$: C, 56.47; H, 3.52; N, 27.45%.
Found: C, 56.11; H, 3.70; N, 27.22%.

13-Preparation of 6-cyano-7-phenyl[1,2,4]triazolo[4,3-a]pyrimidin 5-(8H)-one (**XV**). Compound (**XIV**) (0.01 mol) was fused above its melting point at ≈260°C on heating mantel for about one hour. The solidified product was triturated with ethanol, filtered off and recrystallised from absolute ethanol into white crystals of (**XV**) m.p. 236°C yield 1.3 g., i.r.: 3120 (NH), 2200 (C≡N) and 1660 cm^{-1} (C=O pyrimidinone), ^1H NMR δ 8.8 (s, 1H, CH), δ 7.75 (m, 5H arom) δ 4.8 (s, 1H NH).

Anal. Calcd.: $C_{12}H_7N_5O$: C, 60.75; H, 2.95; N, 29.53%.
Found: C, 60.55; H, 2.87; N, 29.33%.

14-Preparation of 6-cyano 2,8-dihydro-7-phenyl[1,2,4]triazolo-[4,3-a]pyrimidin 3,5-dione (**XVI**). To compound (**IX**) (0.01 mol) dissolved in pyridine (20 ml), ethyl chloro formate (3 ml) was added. The mixture was refluxed for 4 hours, then poured onto cold water. The precipitated product was filtered off and recrystallised from acetic acid to give yellow crystals of (XVI) m.p. 345°C yield 2 g i.r.: 3400 3180 (NH), 2220 (C≡N), 1730 (C=O triazolone) and 1690 cm^{-1} (C=O pyrimidinone).

Anal. Calcd.: $C_{12}H_7N_5O_2$: C, 56.91; H, 2.76; N, 28.66%.
Found: C, 57.72; H, 2.96; N, 28.87%.

15-Preparation of 6-cyano 2,3-dihydro-7-phenyl-3-thioxo[1,2,4]-triazolo[4,3-a]pyrimidin 5(8H) one (**XVII**). A mixture of (**IX**) (0.01 mol), carbon disulphide (5 ml) and alcoholic KOH (5 ml & 1 N) in methanol (30 ml) was refluxed for about 4 hours on a water bath. The precipitated potassium salt was filtered off and refluxed with HCl for one hour where the solid product (**XVII**) was separated out after cooling. The product filtered off and recrystallised from ethanol into yellow crystals m.p. 262°C yield

1.6 g i.r.: 3200 (NH), 2200 (C≡N), 167 (C≡O pyrimidinone) and 1270 cm^{-1} (C═S).
Anal. Calcd.: $C_{12}H_7N_5OS$: C, 53.53; H, 2.60; N, 26.02; S, 11.89%.
Found: C, 53.26; H, 2.69; N, 26.23; S, 12.00%.

16-Preparation of 2-azido-5-cyano-6-phenyl pyrimidin 4(3H) one (**XVIII**). A mixture of (**IX**) (0.01 mol) in ethanol (10 ml) and phosphoric acid (2 ml) was cooled in ice bath to 0–5°C. A cold solution of sodium nitrite (3 gm, in 10 ml H_2O) was added dropwise over a period of 30 minutes while stirring and the mixture was left to stand over-night. The precipitated product was filtered off and recrystallised from ethanol into yellow crystals of (**XVIII**) m.p. 238°C, yield 1.4 g, i.r.: 3120 (NH), 2210 (C═N), 2180 (N_3) and 1670 cm^{-1} (C═O pyrimidinone).
Anal. Calcd.: $C_{11}H_6N_6O$: C, 55.46; H, 2.52; N, 35.29%.
Found: C, 55.57; H, 2.64; N, 35.11%.

17-Preparation of 5-cyano-2(3,5-dimethyl)-1-pyrazoly)-6-phenyl pyrimidin 4(3H) one (**XIX**). A mixture of (**IX**) (0.01 mol) and acetylacetone (0.01 mol) in ethanol (30 ml) was refluxed for 3 hours. The precipitated product was filtered off and recrystallised from ethanol into yellow crystals m.p. 234°C, yield 2 g i.r.: 3100 (NH), 2210 (C≡N) and 1660 cm^{-1} (C═O pyrimidinone), ^1H NMR: δ7.7 (m, 5H, arom.) δ 6.4 (s, 1H—CH), δ4.4 (s, 1H, NH), δ2.6 (s, 3H—CH_3) 2.3 (s, 3H—CH_3).
Anal. Calcd.: $C_{16}H_{13}N_5O$: C, 64.97; H, 4.66: N, 24.05%.
Found: C, 64.71; H, 4.58;N, 24.22%.

Biological Activity: Most of the newly synthesized compounds were screened for bactericidal (*M. luteus, B. cereus, Serratia sp.* and *P. aeruginosa*), fungicidal (*P. duclauxi, A. flavus* and *S. atra*) and bioregulating activity.[5] The compounds were dissolved in ethylene glycol (10 mg/100 ml, 100 ppm) and transferred to filter paper disc (15 mm) diffusion plate methods.[6] Bacterial suspension was prepared by adding 10 ml of sterile distilled water to lo-d-old cultures of the test bacteria grown on a nutrient agar of NA.[7] Also spore suspension was prepared by adding 10 ml sterile distilled water to lo-d-old culture of the test fungi.[8] The detailed screening method used has been described earlier.[5]

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