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Reactions of Pyrimidinonethione Derivatives: Synthesis of 2-Hydrazinopyrimidin-4-one, Pyrimido[1,2-a]-1,2,4-triazine, Triazolo-[1,2-a]pyrimidine, 2-(1-pyrazolo)pyrimidine and 2-Arylhydrazonopyrimidine Derivatives

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6-Aryl-5-cyano-4-pyrimidinon-2-thione derivatives **1a-c** reacted with ethyl iodide to give the corresponded 2-S-ethylpyrimidin-4-one derivatives **2a-c**. Compounds **2a-c** was, in turn, reacted with hydrazine hydrate to give the sulfur free reaction products, **3a-c**. These reaction products were taken as the starting materials for the synthesis of several newly synthesized heterocyclic derivatives. Reactions with several halogenated ketones, esters, chloroacetic acid and chloroacetamide give pyrimidotriazines **8**, **12** and **15** while their reactions with formic acid, acetic acid and carbon disulfide gave the corresponded triazolopyrimidines **17** and **21**. The reaction with both acetyl acetone and ethylacetoacetate gave the corresponded 2-(3',5'-dimethyl-1'-pyrazoly) pyrimidine derivatives **20a-c** and **24a-c** respectively while the reaction with cinnamonitriles **25a-h** afforded the corresponded aryl hydrazopyrimidines **27a-f**. The structures of these reaction products were established based on both elemental analyses and spectral data studies.

Key words : Pyrimidinethione, pyrimidotriazine, triazolopyrimidine and cinnamonitrile

INTRODUCTION

The antifungal, antiviral and antibacterial activity (Koksharova *et al.*, 1992; Leven *et al.*, 1982; Vanden Berghe *et al.*, 1978; Vanden Berghe *et al.*, 1986) of 2-hydrazino pyrimidines **3a-c**, triazolo[1,2-a]pyrimidines **17a-f** and 2-(3',5'-dimethyl-1-pyrazoly)pyrimidines **20a-c** as well as leishmanicidal agents (Ram *et al.*, 1990; Ram *et al.*, 1992) of the annelated pyrimidine derivatives stimulated our interest in the synthesis of several newly synthesized heterocylic derivatives of these ring systems. The 6-aryl-5-cyano-4-pyrimidinone-2-thione derivatives **1a-c** were prepared (Kambe *et al.*, 1979; Ram *et al.*, 1984; Ram *et al.*, 1987) and used as a good reactive reagent to obtain boty 6-aryl-5-cyano-2-S-ethyl-4-pyrimidinone **2a-c** and 6-aryl-5-cyano-2-hydrazino-4-pyrimidin-one **3a-c**.

EXPERIMENTAL

All melting points are uncorrected. IR (KBr discs) were recorded on Pye Unicam SP-1100 spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian EM 390/90 MHz, Gemini 200 MHz and Brucka WP-80 spectrometers using $CDCl_3$, DMSO-d_6 and $(CD_3)_2$ CO as solvents and TMS as an internal standard. Chemical shifts are expressed as δ ppm units. Mass spectra were recorded on Hewlett-Packard GC-MS type 2988 series A using DIP technique at 70 eV. Microanalyses were performed at the Micro-analytical Center of Cairo University using Perkin-Elmer 2400 CHN Elemental Analyzer.

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Synthesis of 2a-c

A solution of each of **1a-c** (0.02 mole) in ethanolic sodium ethoxide (0.01 mole), prepared from the equivalent amounts of sodium metal and ethanol, was treated with ethyl iodide (0.01 mole) and heated under reflux for 5 hours. The solid product obtained on pouring onto cold water was filtered off, washed with water and recrystallized from the proper solvent to give **2a-c** respectively (cf. Tables I and II).

Synthesis of 3a-c

A mixture of **1a-c** or **2a-c** (0.01 mole) wash heated under reflux with an excess of hydrazine hydrate (5 mL) untill the odour of H_2S or C_2H_5SH ceased. The solid products obtained on hot or after cooling were filtered off and recrystallized from proper solvents to give

Table I. Characteriaztion of the newly synthesized compounds

Cpd.	M.p. (°C)	Yield (%)	Cryst. Solvent	Molecular Formula	% of Analysis Calculated/Found				
					C	H	N	S	Cl
2a	270-2	74	Ethanol	$C_{13}H_{11}N_3SO$	60.70 60.7	4.28 4.3	16.34 16.4	12.45 12.4	--- ---
2b	>300	78	DMF	$C_{13}H_{10}N_3SOCl$	53.52 53.5	3.43 3.4	14.4 14.5	10.98 11.0	12.18 12.2
2c	250-2	82	Ethanol	$C_{11}H_9N_3SO_2$	53.44 53.5	3.64 3.7	17.00 17.0	12.96 13.0	--- ---
3a	256	65	Ethanol	$C_{11}H_9N_5O$	58.15 58.2	3.96 4.0	30.84 30.8	--- ---	--- ---
3b	>300	70	DMF	$C_{11}H_8N_5OCl$	50.48 50.5	3.06 3.1	26.77 26.7	--- ---	13.58 13.6
3c	274	84	Ethanol	$C_9H_7N_5O_2$	49.77 50.5	3.23 3.3	32.26 32.2	--- ---	--- ---
8a	296-8	76	Ethanol	$C_{15}H_{11}N_5O_3$	58.25 58.3	35.6 3.6	22.65 22.6	--- ---	--- ---
8b	260	70	Ethanol	$C_{15}H_{10}N_5O_3Cl$	52.40 52.4	2.91 2.9	20.38 20.4	--- ---	10.33 10.3
8c	>300	65	DMF	$C_{13}H_9N_5O_4$	52.17 52.2	3.01 3.0	23.41 23.4	--- ---	--- ---
12a	300	74	DMF	$C_{13}H_9N_5O_2$	58.43 58.4	3.37 3.4	26.22 26.2	--- ---	--- ---
12b	280	64	Ethanol	$C_{13}H_8N_5O_2Cl$	51.74 51.8	2.65 2.7	23.22 23.3	--- ---	11.77 11.8
12c	>300	62	DMF	$C_{11}H_7N_5O_3$	51.36 51.4	27.2 2.7	27.24 27.3	--- ---	--- ---
15a	296-8	74	DMF	$C_{14}H_{11}N_5O$	63.40 63.4	41.5 4.2	26.42 26.4	--- ---	--- ---
15b	290	70	DMF	$C_{14}H_{10}N_5OCl$	56.09 56.1	3.34 3.4	23.37 23.4	--- ---	11.85 11.8
15c	>300	75	DMF	$C_{12}H_9N_5O_2$	56.47 56.5	3.53 3.6	27.45 27.5	--- ---	--- ---
15d	282-4	72	Ethanol	$C_{16}H_{13}N_5O_2$	62.54 62.6	4.23 4.3	22.80 22.8	--- ---	--- ---
15e	270	75	Ethanol	$C_{16}H_{12}N_5O_2Cl$	56.22 56.3	35.1 3.6	20.50 21.0	--- ---	10.40 10.4
15f	296-8	76	Ethanol	$C_{14}H_{11}N_5O_3$	56.57 56.6	3.70 3.7	23.57 23.6	--- ---	--- ---
17a	224-6	82	Ethanol	$C_{12}H_7N_5O$	60.76 61.0	2.95 3.0	29.54 30.0	--- ---	--- ---
17b	292-4	75	Ethanol	$C_{12}H_6N_5OCl$	53.04 53.1	2.21 2.3	25.78 25.8	--- ---	13.08 13.1
17c	>300	79	DMF	$C_{10}H_5N_5O_2$	52.86 52.9	2.20 2.3	30.84 31.0	--- ---	--- ---
17d	164-6	75	Acetic acid	$C_{13}H_9N_5O$	62.15 62.2	3.59 3.6	27.89 27.0	--- ---	--- ---
17e	194-6	74	Acetic acid	$C_{13}H_8N_5OCl$	54.64 54.6	2.80 2.8	24.52 24.5	--- ---	12.43 12.4
17f	185	65	Acetic acid	$C_{11}H_7N_5O_2$	54.77 54.8	2.90 2.9	29.05 29.1	--- ---	--- ---
20a	210	76	Ethanol	$C_{16}H_{13}N_5O$	65.98 66.0	4.47 4.5	24.05 24.1	--- ---	--- ---
20b	286-8	82	Ethanol	$C_{14}H_{11}N_5O_2$	58.99 59.0	3.69 3.7	21.51 22.0	--- ---	10.91 11.0

Table I. Continued

Cpd.	M.p. (°C)	Yield (%)	Cryst. Solvent	Molecular Formula	% of Analysis Calculated/Found				
					C	H	N	S	Cl
20c	240	85	Ethanol	$C_{14}H_{11}N_5O_2$	59.79 58.8	3.91 4.0	24.91 25.0	--- ---	--- ---
21a	296-8	62	Acetic acid	$C_{12}H_7N_5OS$	53.53 54.0	26.0 2.6	26.02 26.1	11.90 12.0	--- ---
21b	210-2	65	Ethanol	$C_{12}H_6N_5OSCl$	47.45 47.5	1.98 2.0	23.06 23.1	10.54 10.6	11.70 11.7
21c	256-8	78	Ethanol	$C_{10}H_5N_5O_2S$	50.19 50.2	1.93 2.0	27.03 27.1	12.36 12.4	--- ---
24a	280	82	Ethanol	$C_{15}H_{11}N_5O_2$	61.43 61.5	3.75 3.8	23.89 23.9	--- ---	--- ---
24b	260	74	Ethanol	$C_{15}H_{10}N_5O_2Cl$	54.96 55.0	3.05 3.1	21.37 21.4	--- ---	10.84 10.9
24c	214	79	Ethanol	$C_{13}H_9N_5O_3$	55.12 55.1	3.18 3.2	24.73 24.8	--- ---	--- ---
27a	297-9	72	Acetic acid	$C_{18}H_{13}N_5O$	68.57 68.6	4.13 4.2	22.22 22.3	--- ---	--- ---
27b	312	82	Acetic acid	$C_{18}H_{12}N_5OCl$	61.80 61.8	3.43 3.4	20.03 20.1	--- ---	10.16 10.2
27.c	>300	65	DMF	$C_{18}H_{12}N_5OCl$	61.80 61.8	3.43 3.5	20.03 20.0	--- ---	10.16 10.1
27d	310	75	Acetic acid	$C_{18}H_{11}N_5OCl$	56.25 56.2	2.86 2.9	18.23 18.3	--- ---	18.49 18.5
27e	295-7	82	Acetic acid	$C_{16}H_{11}N_5O_2$	62.95 63.0	3.61 3.7	22.95 23.0	--- ---	--- ---
27f	>300	78	DMF	$C_{16}H_{10}N_5O_2Cl$	56.55 56.6	2.95 3.0	20.62 20.6	--- ---	10.46 10.5

3a-c respectively (cf. Tables I and II).

Synthesis of 8a-c, 12a-c and 15a-f

A solution of each of **3a-c** (0.01 mole) and each of ethyl-α-chloroacetoacetate (**4**), chloroethylacetate (**9a**), chloroacetamide (**9b**), chloroacetic acid (**9c**), chloroacetone (**13a**) and α-chloroacetyl acetone (**13b**) in sodium methoxide (0.01 atom of sodium metal in 30 ml of methanol) was heated under reflux for 7 hours. The reaction mixture was cooled and poured onto ice-cold water. The solid products obtained after acidification with concentrated HCl were filtered off, washed with water and then recrystallized from proper solvent to give **8a-c**, **12a-c** and **15a-f** respectively (cf. Tables I and II).

Synthesis of 17a-f

A mixture of each of **3a-c** (0.01 mole) and each of acetic anhydride (20 mL) and formic acid (20 mL) was heated under reflux for 7 hours. The solid products obtained after pouring onto ice-cold water were filtered off, washed with water and then recrystallized from the proper solvent to give **17a-f** respectively (cf. Tables I and II).

Synthesis of 20a-c

A mixture of each of **3a-c** (0.01 mole) and acetyl acetone (**18**) (0.01 mole) in methanol-acetic acid mixture (1:3) was heated under reflux for 5 hours. The solid products obtained after pouring onto ice-cold water were filtered off and recrystallized from the proper solvent to give **20a-c** respectively (cf. Tables I and II).

Synthesis of 21a-c

A solution of each of **3a-c** (0.01 mole) in pyridine (30 ml) was treated with carbon disulphide. The reaction mixture was heated under reflux for 5 hours. The reaction mixture was cooled, poured onto ice-cold water and then acidified with concentrated hydrochloric acid. The solid products obtained were filtered off, washed with water and then recrystallized from the proper solvent to give **21a-c** respectively (cf. Tables I and II).

Synthesis of 24a-c and 25a-f

A solution of each of **3a-c** (0.01 mole) in methanol (30 mL) containing catalytic amounts of triethylamine

Table II. IR and ^{1}H-NMR Spectral data

Comp.	IR (cm^{-1})	^{1}H-NNR (δppm)
2a	3185 (NH); 3070 (aromatic C-H); 2985, 2972 (aliphatic C-H); 2214 (CN); 1695 (CO amide); 1620 (C=N) and 1600 (C=C)	0.92 (t, 3H, CH_3CH_2); 3,4 (q, 2H, CH_3CH_2); 5.3 (s, br, 1H, NH of pyrimidinone) and 7.3~8.2 (m, 5H, ArH's)
2b	3187 (NH); 3070 (aromatic C-H); 2982, 2968 (aliphatic C-H); 1984 (CO amide); 1618 (C=N) and 1603 (C=C)	1.0 (t, 3H, CH_3 CH_2); 3.9 (q, 2H, CH_3 CH_2); (s, br., 1H, NH of pyrimidinone) and 7.1~7.9 (m, 3H, Ar H, s)
2c	3182 (NH); 2983, 2975 (aliphatic C-H); 2213 (CH); 1685 (CO amide); 1617 (C=N) and 1600 (C=C)	0.9 (t, 3H, CH_3 CH_2); 3.4 (q, 2H, CH_3 CH_2); 5.2 (s, br., ^{1}H, NH of pyrimidinone) and 6.4~7.2 (m, 3H, Furyl).
3a	3395, 332, 3270, 3180 (NH_2 and NH); 3079, (aromatic CH); 2218 (CN); 1694 (CO amide); 1615 (C=N) and 1602 (C=C)	5.0 (s, br., 1H, NH of pyrimidinone); 6.2 (s, br., 1H, NH hydrazino); 7.1~8.2 (m, 5H, ArH's) and 9.1 (s, br., 2H, NH_2 hydrazino)
3b	3390, 3325, 3280, 3182 (NH_2 and NH); 3074 (aromatic CH); 2217 (CN); 1690 (CO amide); 1612 (C=N) and 1600 (C=C)	4.9 (s, br., 1H, NH of pyrimidinone); 6.4 (s, br., 1H, NH hydrazino); 7.2~7.9 m, 4H, Ar H's) and 9.3 (s, br, 2H, NH_2)
3c	3390, 3318, 3259, 3176 (NH_2 and NH); 3330 (CN); 1689 (CO amide); 1617 (C=N) and 1600 (C=C)	4.8 (s, br., 1H, NH of pyrimidinone); 5.9 (s, br., 1H, NH hydrazino); 6.4~7.0 (m, 3H, furyl H's and 8.6 (s, br, 2H, NH_2 hudrazino)
8a	3350 (OH enolic); 3225, 3188 (two NH) 2218 (CH); 1710 (acetyl CO); 1685 (CO amide); 1610 (C=N) and 1600 (C=C)	1.3 (s, 3H, CO CH_3); 6.4 (s, br., 2H two NH); 7.2~8.1 (m, 5H, Ar H's) and 10.1 (s, br., 1H, OH enolic).
8b	3362 (OH enolic); 3232, 3185 (two NH) 2217 (CN); 1710 (CO acetyl); 1685 (CO amide); 1615 (C=N) and 1601 (C=C)	1.5 (s, 3H, CO CH_3); 5.8 (s, br., 2H, two NH); 7.1~8.1 (m, 4H, Ar H's) and 10.4 (s, br., 1H, OH enolic)
8c	3358 (OH enolic); 3220, 3180 (Two NH); 2215 (CN); 1715 (CO acetyl); 1690 (CO amide); 1612 (C=N) and 1600 (C=C)	1.5 (s, 3H, $COCH_3$); 6.2~6.9 (m, 5H, Furyl and two NH Protons and 10.4 (s, br., 1H, OH enolic)
12a	3362 (OH enolic); 3227, 3189 (Two NH); 3079 (aronatic; CH); 2217 (CN); 1712 (CO acetyl); 1613 (C=N) and 1600 (C=C)	5.1 (s, 1H, triazine H-6); 6.2 (s, br., 2H, two NH); 7.0-8.1 (m, 5H, Ar H's) and 10.2 (s, br., 1H, OH enolic)
12b	3370 (OH enolic); 3230, 3195 (two NH); 2213 (CN); 1690 (CO amidic); 1610 (C=N) and 1600 (C=C)	5.5 (s, 1H, triazine H-6); 6.4 (s, br., 2H, two NH), 7.1-8.2 (m, 4H, Ar H's) and 10.3 (s, br., 1H, OH enolic)
12c	3356 (OH enolic); 3231, 3192 (two NH); 2219 (CN); 1687 (CO amidic); 1617 (C=N) and 1602 (C=C)	5.0 (s, 1H, triazine H-6); 5.7 (s, br., 2H, two NH), 6.2~6.9 (m, 6H, fury H's) and 10.5 (s, br., 1H, OH enolic)
15a	3220, 3187 (two NH); 3075 (aromatic CH); 2978, 2890 (aliphatic CH); 2215 (CN); 1685 (CO amide) 1610 (C=N) and 1600 (C=C)	1.3 (2, 3H, CH_3), 5.3 (s, 1H, triazine H-6); 6.4 (s, br., 2H, two NH) and 7.2-8.1 (m, 5H, Ar Hs)
15b	3227, 3182 (two NH); 3082 (aromatic CH); 2979, 2892 (aliphatic CH); 2218 (CN); 1682 (CO amide); 1614 (C=N) and 1600 (C=C)	1.1 (s, 3H, CH_3), 5.1 (s, 1H, triazine H-6); 6.2 (s, br., 2H, two NH) and 7.0~8.2 (m, 4H, Ar H's)
15c	3230, 3193 (two NH); 2973, 2877 (aliphatic CH); 2220, 2890 (aliphatic CH); 2213 (CN); 1710 (CO acetyl); 1692 (CO amide); 1608 (C=N) and 1600 (C=C)	1.4 (s, 6H, two CH_3; 6.3 (s, br., 2H, two NH) and 7.2~8.3 (m, 4H, Ar H's)
15d	3222, 3182 (two NH); 3070 (aromatic CH); 2972, 2890 (aliphatic CH); 2213 (CN); 1710 (CO acetyl); 1692 (CO amide); 1608 (C=N) and 1600 (C=C)	1.4 (s, 6H, two CH_3); 6.3 (s, br., 2H, two NH) and 7.2~8.3 (m, 4H, Ar, H's)
15e	3225; 3180 (two NH); 3082 (aromatic CH); 2980, (aliphatic CH); 2215 (CN); 1715 (CO acetyl); 1684 (C=N) and 1602 (C=C)	1.6 (s, 6H two CH_3); 6.1 (s, br., 2H, two NH); and 7.0~8.1 (m, 4H, Ar H's)
15f	2317, 3192 (two NH); 2985, 2878 (aliphatic CH); 2215 (CN); 1712 (Co acetyl); 1689 (CO amide); 1618 (C=N) and 1600 (C=C)	1.4 (S, 6H, two CH_3); 6.2~6.9 (m, 5H, furyl and two NH protons)
17a	3180 (NH); 2215 (CN); 1690 (CO amide); 1608 (C=N) and 1600 (C=N)	4.9 (s, 1H, triazole H-5); 7.2-8.3 (m, 5H, Ar H's) and 8.2 (s, br., 1H, NH)
17b	3182 (NH); 3079 (aromatic CH); 2217 (CN); 1685 (CO amide); 1610 (C=N) and 1600 (C=C)	4.6 (s, 1H, triazole H-5); 7.0~8.1 (m, 4H, Ar H's) and 8.7 (s, br., 1H, NH) triazole

Table II. Continued

Comp.	IR (cm^{-1})	^{1}H-NNR (δppm)
17c	3180 (NH); 2213 (CN); 1692 (CO amide); 1612 (C=N) and 1600 (C=C)	4.8 (s, 1H, triazole H-5); 6.2~6.9 (m, 3H, furyl H'S) and 8.3 (s, br., 1H, NH)
17d	3192 (NH); 3069 (aromatic CH); 2987, 2894 (aliphatic CH); 2215 (CN); 1690 (CO amide); 1612 (C=N) and 1600	1.2 (s, 3H, CH_3); 7.2~8.4 (m, 6H, Aromatic and NH)
17e	3189 (NG); 3076 (aromatic CH); 2989, 2878 (aliphatic CH); 2217 (CN); 1617 (C=N) an d1602 (C=C)	1.4 (s, 3H, CH_3); 7.1~8.2 (m, 4H, Ar H's) and 8.7 (s, br., 1H, NH)
17f	3182 (NH); 2978, 2868 (aliphatic CH); 2217 (CN); 1686 (CO amide); 1618 (C=N) and 1600 (C=C)	1.3 (s, 3H, CH_3); 6.2~6.9 (m, 3H, fury H's) and 8.5 (s, br., 1H, NH)
20a	3222 (NH); 3083 (aromatic CH); 2984, 2897 (aliphatic CH); 2218 (CN); 1693 (CO amide); 1615 (C=N) and 1601 (C=C)	1.5 (s, 6H, two CH_3) and 7.2~8.6 (m, 7H, Aromatic, NH of pyrimidinone and pyrazole H-4 protons)
20b	3215 (NH); 3078 (aromatic CH); 2980, 2890 (aliphatic CH) 2213 (CN); 1685 (CO amide); 1612 (C=N) and 1600 (C=C)	1.3 (s, 6H, two CH_3) and 7.1~8.5 (m, 6H, Aromatic, NH of pyrimidinone and pyrazole H-4 protons)
20c	3196 (NH); 2979, 2873 (aliphatic CH); 2215 (CN); 1687 (CO amide); 1613 (C=N) and 1600 (C=C)	1.4 (s, 6H, two CH_3); 6.2~6.8 (m, 3H, furyl H's) and 8. 6 (s, br., 2H NH of pyrimidinone and pyrazole H-4)
21a	3198, 3178 (two NH); 3065 (aromatic CH); 2215 (CN); 1685 (CO amide); 1608 (C=N) and 1600 (C=C)	6.2 (s, br., 2H, two NH) and 7.2~8.3 (m, 5H, Ar H's)
21b	3189, 3172 (two NH); 3078 (aromatic CH); 2217 (CN); 1690 (CO amide); 1613 (C=N) and d1600 (C=C)	5.9 (s, br., 2H, two NH) and 7.0~8.1 (m, 4H, Ar H's)
21c	3190, 3169 (two NH); 2221 (CN); 1687 (CO amide); 1615 (C=N) and 1600 (C=C)	6.0 (s, br., 2H, two NH) and 6.3~6.9 (m, 3H, fury H's)
24a	3197, 3175 (two NH); 3080 (aromatic CH); 2974 2892 (aliphatic CH), 2220 (CN); 1693 (CO amide); 1613 (C=N) and 1602 (C=C)	1.3 (s, 3H, CH_3 and 7.1~8.2 (m, 8H, aromatic, two NH of pyrazole and pyrazole H-4)
24b	3190, 3169 (two NH); 3078 (aromatic CH); 2982, 2879 (aliphatic CH); 2218 (CN); 1695 (CO amide); 1610 (C=N)	1.5 (s, 3H, CH_3) and 7.2~8.4 (m, 7H, aromatic, two NH of pyrazole and pyrazole H-4)
24c	3220, 3185 (two NH); 3080 (aromatic CH); 2985, 2897 (aliphatic CH); 2218 (CN); 1687 (CO amide); 1610 (C=N) and 1600 (C=C)	1.2 (s, 3H, CH_3) and 6.4~7.8 (m, 6H, Furyl, two NH protons and pyrazole H-4)
27a	3200, 3182 (two NH); 3070 (aromatic CH); 2218 (CN); 1690 (CO amide); 1607 (C=N) and 1600 (C=C)	5.3 (s, 1H, CH=N-); 7.1~8.2 (m, 11H, aromatic and NH of pyrimidinone protons) and 9.7 (s, br., 1H,=H-NH-)
27b	3232, 3197 (two NH); 3084 (aromatic CH); 2222 (CN); 1692 (CO amide); 1613 (C=N) and 1601 (C=C) and 1600 (C=C)	5.5 (s, 1H, -CH=N-); 7.2~8.1 (m, 10H, aromatic and pyrimidinone NH protons and 9.9 (s, br., 1H, -N-NH-)
27c	3228, 3187 (tew NH); 3078 (aromatic CH); 2220 (CN); 1689 (CO amide); 1613 (C=N) and 1601 (C=C)	5.3 (s, 1H, -CH=N-); 7.0~8.1 (m, 10H, aromatic and pyrimdinone NH protons) and 10.1 (s, ber., 1H=N-NH-)
27d	3220, 3179 (two NH); 3082 (aromatic CH); 2218 (CN); 1685 (CO amide); 1615 (C=N) and 1604 (C=C)	5.2 (s, 1H, CH=N-); 7.1~8.0 (m, 9H, aromatic and pyrimidinone NH protons) and 9.8 (s, br., 1H, =N-NH-)
27e	3220, 3195 (two NH); 3070 (aromatic CH); 2218 (CN); 1685 (CO amide); 1610 (C=N) and 1600 (C=C)	5.2 (s, 1H, -CH=N-); 6.3~6.8 (m, 3H, Furyl protons); 7. 2~8.3 (m, 6H, aromatic and NH of pyrimidinone protons) and 9.7 (s, br., 1H, =N-NH-)
27f	3222, 3189 (two NH); 3084 (aromatic CH); 1693 (CO amide); 1615 (C=N) and 1603 (C=C)	5.1 (s, 1H, -CH=N-); 6.2~6.7 (m, 3H, furyl H's); 7.1~8. 2 (m, 5H, andpyrimidinone NH protons) and 9.7 (s, br., 1H, =N-NH-)

(0.5 mL) was treated with each of ethylacetoacetate (**22**) and each of **25a-h** or **26a,b**. The reaction mixture was heated under reflux for 5 hours. The solid products obtained on hot or after cooling were filtered off and recrystallized from the proper solvent to give **24a-c** and **27a-f** respectively (cf. Tables I and II).

RESULTS AND DISCUSSION

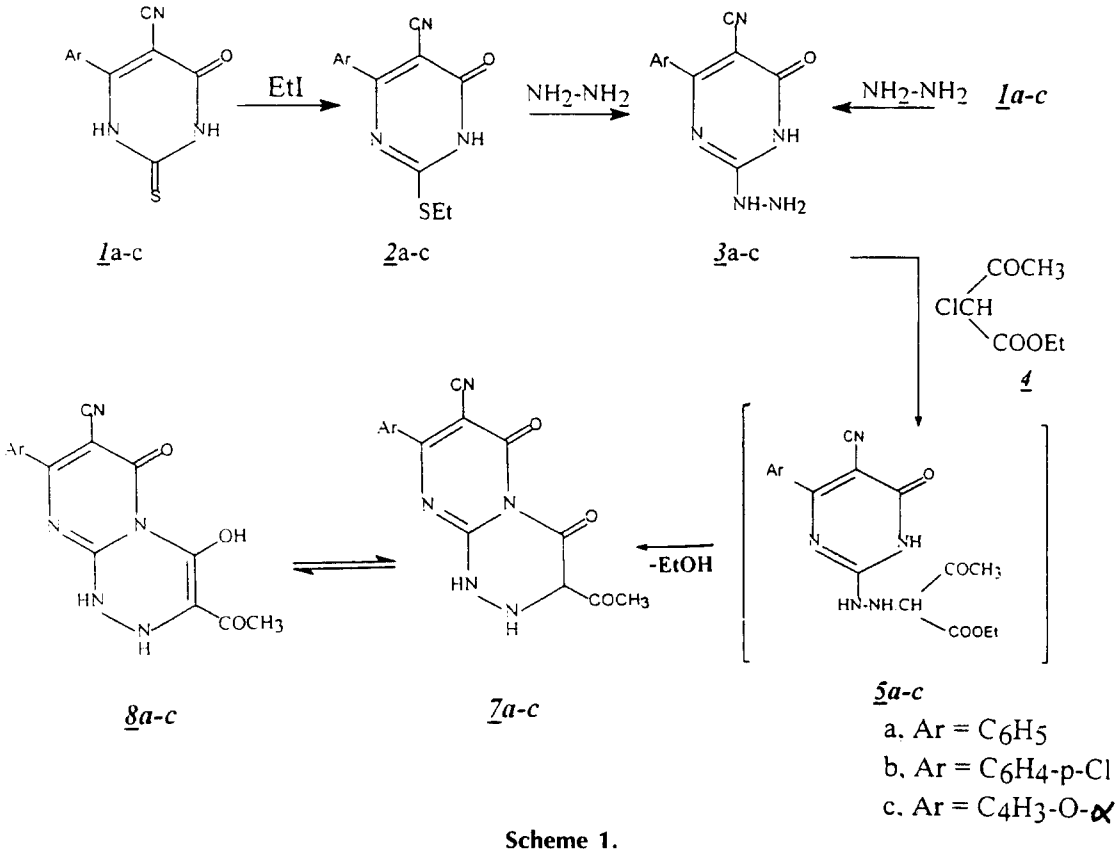
It has been found that 6-aryl-5-cyano-4-pyrimidinone-

2-thione derivatives **1a-c** reacted with ethyl iodide in sodium ethoxide to give the 2-S-ethyl derivatives **2a-c**. The structures of **2a-c** were established based on both elemental analyses and spectral data studies (cf. Tables I and II). Each of **2a-c** reacted with hydrazine hydrate to give the sulfur free reaction products **3a-c**. Compounds **3a-c** were prepared through another route where **1a-c** reacted with hydrazine hydrate to give the same reaction products **3a-c**. The reaction product given from the two routes are identical in all aspects m. p., mixed m. p., IR, ^{1}H-NMR and mass spectral., data as well as elemental analyses confirm the given structures **3a-c** (cf. Tables I and II). Moreover, the mass spectrum of **3a** as a typical example gave m/z=227 which correspondede to the exact molecular weight of a molecular formula $C_{11}H_9N_5O$ (cf. Scheme 1).

Considering all the above data, these reaction products were formulated as 6-aryl-5-cyano-2-hydrazino-4-pyrimidinone derivatives **3a-c**. Structures **3a-c** were supported also by sulfur test, where no sulfur found and the sulfur free reaction products were considered.

Compounds **3a-c** were taken as a good starting materials for the present study owing to the presence more than one active site in each of them. Thus, it has been found that **3a** reacted with ethyl-α-chloroacetoacetate (**4**) in methanolic sodium methoxide to give the non-isolable products formed through the loss of hydrogen chloride **5a**. The non-isolable products **5a** was most probably cyclized by loosing of ethanol molecule to give **7a** which could be enolized to **8a**. The IR (cm^{-1}) of this reaction product showed the presence of the bands at 3350 (OH enol), 3225 and 3188 (NH), 2218 (CN), 1710 (CO ketone) and 1685 (CO amide). Its ^{1}H-NMR (δ) revealed the signals corresponded to 1.3 (s, 3H, CH_3CO), 6.4 (s, br., 2H, two NH), 7.2 ~8.1 (m, 5H, ArH's) and 10.1 (s, 1H, enol OH). Based on these spectral data, the reaction product was formulated as pyrimide[1,2-a]-1,2,4-triazinole derivative **8a**. Moreover, the mass spectrum of **8a** gave m/z=309 which corresponded to the molecular weight of a molecular formula $C_{15}H_{11}N_5O_3$ of the assigned structure **8a** (cf. Tables I, II and Scheme 1). In a similar way, compounds **3b,c** reacted also, with ethyl-α-chloroacetoacetate (**4**) under the same experimental conditions to give the non-isolable reaction products **5b, c** which are readily cyclized to give pyrimido[1,2-a]-1,2,4-triazinole derivatives **8b,c** rather than pyrimido [1,2-a]-1,2,4-triazinone derivatives **7b,c**. The structures **8b,c** were established based on elemental analyses, IR (cm^{-1}) and ^{1}H-NMR (δ) spectral data (cf. Tables I, II and Scheme 1).

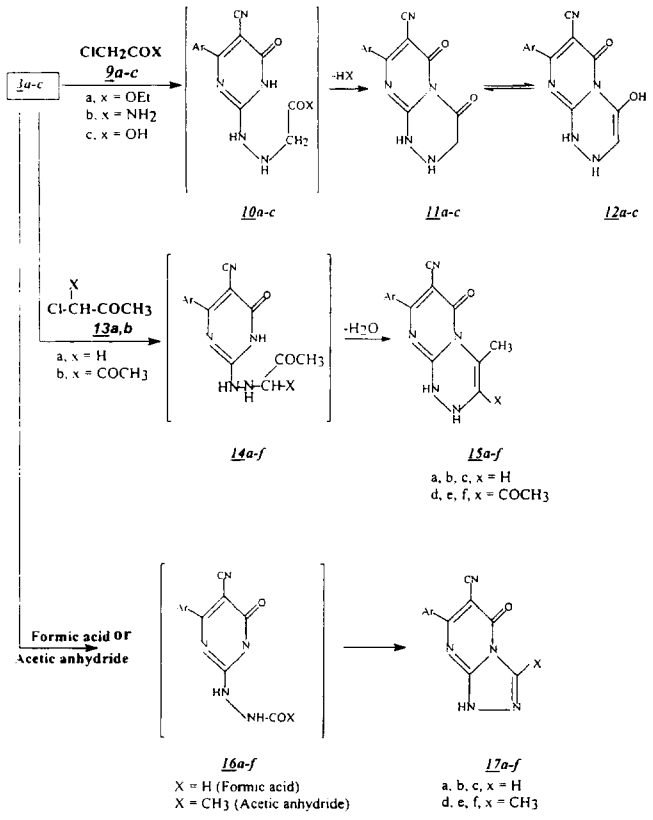
Compounds **3a-c** also, reacted with each of ethyl chloroacetate (**9a**), chloroacetamide (**9b**) and chloroacetic acid (**9c**) in methanolic sodium methoxide to



Scheme 1.

give the non-isolable reaction products **10a-c** via the loss of hydrogen chloride molecule in each case. The non-isolable reactionn products **10a-c** were most probably cyclized through the loss of ethanol, ammonia or water molecules according to the reagent used (cf. Scheme 2). It is remarkable to report here that, each of **3a-c** reacted with all the reagents **9a-c** to give one and the same reaction product. The IR (cm^{-1}) of this reaction product showed the bands of OH, NH, CN and CO groups. Moreover, its ^{1}H-NMR revelaed the signals of aromatic, NH, triazine H-6 and OH protons. Considering all the above spectral data and elemental analyses, these reaction products were formulated as pyrimido[1,2-a]-1,2,4-triazinole derivatives **12a-c** rather than the pyrimido[1,2-a]-1,2,4-triazinone derivatives **11a-c**. A further confirmation of **12a-c** structures were given from the mass sepctrum of **12b** as a typical example gave m/z=301 which corresponded to the molecular weight of a molecular formula $C_{13}H_8N_5O_2Cl$ of the assigned structure **12b** (cf. Scheme 2, Tables I and II).

In a similar behaviour compounds **3a-c** react with both chloroacetone (**13a**) and α-chloroacetylacetone (**13b**) to give the non-isolable reaction products **14a-f** respectively via the loss of hydrogen chloride molecule in each case. The non-isolable reaction products **14a-f** were cyclised most probably through the loss of water molecule in each case to give the reaction products **15a-f** respectively. The IR (cm^{-1}) of **15a-c** showed the bands of NH, CN and amidic CO groups while their ^{1}H-NMR (δ) revealed the signals of CH_3, aromatic or furyl, triazine H-6 and NH protons (cf. Tables I and II). The mass spectrum of **15c** as a selective example gave m/z=255 which corresponded to the molecular weight of a molecular formula $C_{12}H_9N_5O_2$ of the assigned structure. Considering all the above spectral data and elemental analyses, **15a-c** were formulated as pyrimido[1,2,-a]1,2,4-triazine derivatives. The IR (cm^{-1}) io **15d-f** showed the bands of NH, CN, amidic CO and ketonic CO while their ^{1}H-NMR spectra revealed the signals corresponded to CH_3, CH_3CO, NH and aromatic or furyl protons (cf. Table II). Moreover, the mass spectrum of **15d** as an example gave m/z=307 which corresponded to the molecular weight of the formula $C_{16}H_{13}N_5O_2$ of the assigned structure (cf. Scheme 2).

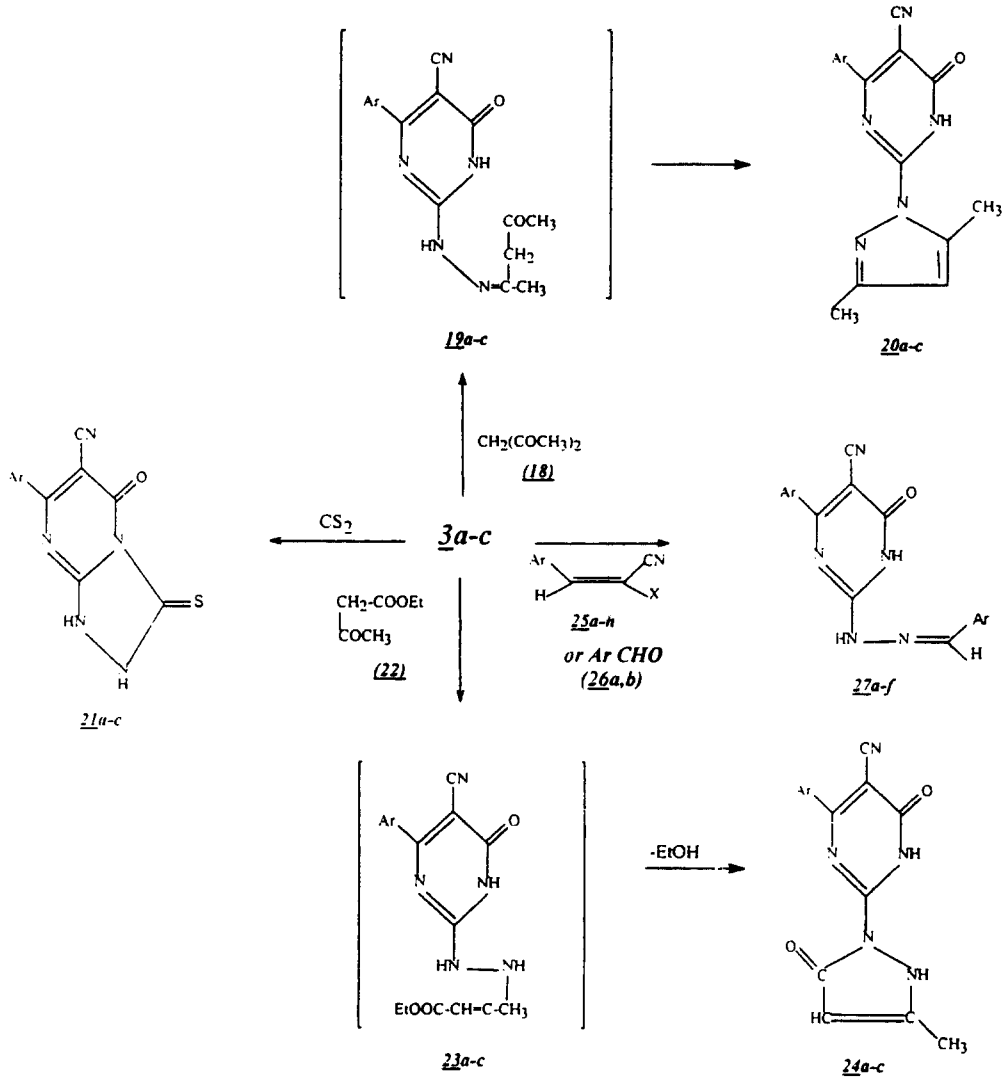


Scheme 2.

The synthons **3a-c** also, reacted with both formic acid and acetic anhydride to give the corresponded 1, 2,4-triazolo[1,2-a]pyrimidinone derivatives **17a-f** respectively. Trials to obtain the compounds **16a-c** are failed under several conditions. The structures **17a-f** were established based on elemental analyses, IR and ^{1}H-NMR spectra data (cf. Tables I and II). A further confirmation of **17a-f** were given from the mass spectral data, a mass spectrum of each of **17a** and **17f** as a selective example gave m/z=237 and 241 respectively which represented the molecular weights of the molecular formulae $C_{12}H_7N_5O$ and $C_{11}H_7N_5O_2$ of the assigned structures respectively (cf. Scheme 2).

The synthetic potential of the compounds **3a-c** was further investigated through their reaction with each of acetylacetone (**18**) and ethylacetoacetate (**22**) as an active methylene containing reagents. Thus, it has been found that 5-cyano-2-hydrazino-6-phenyl-4-pyrimidinone (**3a**) reacted with each of acetylacetone (**18**) and ethylacetoacetate (**22**) in methanol-acetic acid mixture (1:3) to give the non-isolable reaction products **19a** and **23a** respectively. It is remarkable to report here that all attempts to isolate compounds **19a** or **23a** are failed. The IR (cm^{-1}) of the reaction products showed the bands of NH, CN and amidic CO groups. Their ^{1}H-NMR (δ) revealed the signals of CH_3, pyrazole H-4, phenyl and NH protons (cf. Tables I, II and Scheme 3). Moreover, the mass spectra of **20a** and **24a** as a selective examples gave m/z=291 and 293 respectively which represented the molecular weights of the molecular formulae $C_{16}H_{13}N_5O$ and $C_{15}H_{11}N_5O_2$ of the assigned structures respectively. Based on the above data the reaction products were formulated as 5-cyano-2-(3',5'-dimethyl-1'-pyrazoly)-6-phenyl-4-pyrimidinone (**20a**) and 5-cyano-2-(3-methyl-5-pyrazolon-1-yl)-6-phenyl-4-pyrimidinone (**24a**) respectively.

In a similar manner, compounds **3b,c** reacted under the same experimental conditions with both acetyl acetone (**18**) and ethyl acetoacetate (**22**) to give the



25	Ar'	X
a	C_6H_5	CN
b	C_6H_4-p-Cl	CN
c	C_6H_5	COOEt
d	C_6H_4-p-Cl	COOEt
e	C_6H_5	CONH2
f	C_6H_4-p-Cl	CONH2
g	C_6H_5	CSNH2
h	C_6H_4-p-Cl	CSNH2

27	Ar'	Ar
a	C_6H_5	C_6H_5
b	C_6H_4-p-Cl	C_6H_5
c	C_6H_5	C_6H_4-p-Cl
d	C_6H_4-p-Cl	C_6H_4-p-Cl
e	C_6H_5	C_4H_3-O-α
f	C_6H_4-p-Cl	C_4H_3-O-α

Scheme 3.

corresponding 2-(1'-pyrazoly)pyrimidinone derivatives **20b,c** and 2-(1'-pyrazolonyl)pyrimidinone derivatives **24b,c**. Their structures were also established based on elemental analyses, IR and ^{1}H-NMR spectral data (cf. Scheme 3, Table I and II).

The reactions of **3a-c** were also extended towards the measurment of their synthetic potential. Thus, each of **3a-c** reacted with carbon disulphide in pyridine to give a reaction product **21a-c** via the loss of hydrogen sulphide molecule. The IR (cm^{-1}) of these reaction products showed the bands of NH, CN and CO amidic groups in each case. Moreover ^{1}H-NMR (δ) revealed the signals of NH, aromatic and furyl protons. Moreover, the mass spectrum of **21a** as a selective example gave m/z=269 which represented the molecular weight of a molecular formula $C_{12}H_7N_5SO$ of the assigned structure. Based on both elemental analyses and the above spectral data sdtudies, these reaction

products were formulated as 1,2,4-triazolo[1,2-a]pyrimidinone derivatives **21a-c** respectively (cf. Scheme 3).

A further and final demonstration of **3a-c** activity was achieved through their reaction with both cinnamonitrile derivatives **25a-h** or aromatic aldehydes **26a, b**. Thus, it has been found that **3a** reacted with the cinnamonitrile derivatives **25a,b** or aromatic aldhyde **26a, b** in acetic acid to give the same reaction products. These reaction products are identical in all aspects, m. p. elemental analyses, IR and ^{1}H-NMR. Moreover, their mass spectra gave m/z=315 and 350 which corresponded to the molecular weights of the molecular formulae $C_{18}H_{13}N_5O$ and $C_{18}H_{12}N_5OCl$ of the assigned structure (cf. Scheme 3). Based on all the above data these reaction products were represented as the arylidene group exchange reaction products. These reaction products were formulated as 2-arylidenehydrazone-6-phenyl-5-cyano-4-pyrimidinone (**27a,b**). The structures the above mentioned arylidene group exchange reaction products proved by the reaction of the each of **25c-h** with **3a** under the same reaction experimental conditions to give the arylidene group exchanged reaction products **27a,b**. These reaction products were identical in all aspects with the **27a,b** given through the reaction of each of **25a,b** or **26a,b** with **3a** (cf. Tables I, II and Scheme 3).

In a similar experimental reaction conditions each of **3b,c** reacted with each of cinnamonitrile derivatives **25a-h** or aromatic aldhydes (**26a,b**) to give the arylidene group exchanged reaction products **27c-f**. The structures of **27c-f** were established based on elemental analyses, IR (cm^{-1}) and ^{1}H-NMR (δ) spectral data. Moreover, their mass spectra gave m/z=349, 384, 305 and 339 which represented the exact molecular weights of the molecular formulae $C_{18}H_{12}N_5OCl$ and $C_{18}H_{11}N_5OCl_2$, $C_{16}H_{11}N_5O_2$ and $C_{16}H_{10}N_5O_2Cl$ of the assigned structures (cf. Scheme 3, Tables I and II).

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